

=> s human? (5a) papillom? (5a) virus? or HPV or hpv16 or hpv18

FILE 'AIDSLINE'

105607 HUMAN?  
583 PAPILLOM?  
36905 VIRUS?  
170 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
315 HPV  
10 HPV16  
4 HPV18  
L1 395 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'BIOSIS'

3363491 HUMAN?  
13020 PAPILLOM?  
298047 VIRUS?  
1992 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
3851 HPV  
346 HPV16  
112 HPV18  
L2 5211 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'CANCERLIT'

731480 HUMAN?  
13687 PAPILLOM?  
83665 VIRUS?  
1210 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
4125 HPV  
342 HPV16  
97 HPV18  
L3 4725 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'CAPLUS'

614928 HUMAN?  
4536 PAPILLOM?  
165017 VIRUS?  
1753 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
1434 HPV  
285 HPV16  
90 HPV18  
L4 2064 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'CEN'

1678 HUMAN?  
3 PAPILLOM?  
274 VIRUS?  
0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
0 HPV  
0 HPV16  
0 HPV18  
L5 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'DISSABS'

52946 HUMAN?  
251 PAPILLOM?  
8823 VIRUS?  
19 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
107 HPV  
10 HPV16  
0 HPV18  
L6 119 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'DRUGB'

82659 HUMAN?  
407 PAPILLOM?  
21940 VIRUS?  
0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
43 HPV  
0 HPV16  
0 HPV18  
L7 43 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'DRUGLAUNCH'

1167 HUMAN?  
4 PAPILLOM?  
451 VIRUS?  
0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
0 HPV

8/170344  
8/95



0 HPV16  
 0 HPV18  
 L8 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'DRUGNL'  
 737 HUMAN?  
 38 PAPILLOM?  
 275 VIRUS?  
 22 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 23 HPV  
 0 HPV16  
 0 HPV18  
 L9 32 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'DRUGU'  
 124166 HUMAN?  
 846 PAPILLOM?  
 22736 VIRUS?  
 101 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 337 HPV  
 21 HPV16  
 6 HPV18  
 L10 387 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'EMBASE'  
  
 2688991 HUMAN?  
 10578 PAPILLOM?  
  
 244295 VIRUS?  
 862 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 3844 HPV  
 290 HPV16  
 85 HPV18  
 L11 4103 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'IFIPAT'  
 31479 HUMAN?  
 73 PAPILLOM?  
 3663 VIRUS?  
 19 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 30 HPV  
 2 HPV16  
 2 HPV18  
 L12 39 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'IPA'  
  
 16694 HUMAN?  
 46 PAPILLOM?  
 2186 VIRUS?  
 5 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 46 HPV  
 1 HPV16  
 1 HPV18  
 L13 49 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'JICST-EPLUS'  
 705555 HUMAN?  
 1792 PAPILLOM?  
 29100 VIRUS?  
 162 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 433 HPV  
 31 HPV16  
 6 HPV18  
 L14 535 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'LIFESC'  
  
 169120 HUMAN?  
 3027 PAPILLOM?  
 96803 VIRUS?  
 1650 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 1428 HPV  
 177 HPV16  
 49 HPV18  
 L15 1943 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18  
  
 FILE 'MEDLINE'  
  
 5428293 HUMAN?



14299 PAPILLOM?

226558 VIRUS?  
1060 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
4029 HPV  
298 HPV16  
89 HPV18  
L16 4565 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'NAPRALERT'  
12331 HUMAN?  
57 PAPILLOM?  
1420 VIRUS?  
3 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
0 HPV  
0 HPV16  
0 HPV18  
L17 3 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'NLDB'  
76966 HUMAN?  
706 PAPILLOM?  
15292 VIRUS?  
232 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
411 HPV  
23 HPV16  
5 HPV18  
L18 525 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PHIC'  
142 HUMAN?  
2 PAPILLOM?  
37 VIRUS?  
1 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
6 HPV  
0 HPV16  
0 HPV18  
L19 6 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PHIN'  
15635 HUMAN?  
279 PAPILLOM?  
5678 VIRUS?  
101 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
139 HPV  
2 HPV16  
0 HPV18  
L20 196 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PNI'  
8901 HUMAN?  
188 PAPILLOM?  
2654 VIRUS?  
37 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
95 HPV  
1 HPV16  
0 HPV18  
L21 116 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'SCISEARCH'  
521146 HUMAN?  
8385 PAPILLOM?  
160283 VIRUS?  
732 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
2557 HPV  
233 HPV16  
85 HPV18  
L22 3107 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'TOXLINE'  
845572 HUMAN?  
3914 PAPILLOM?  
52603 VIRUS?  
161 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
535 HPV  
35 HPV16  
13 HPV18  
L23 626 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18



FILE 'TOXLIT'

205478 HUMAN?  
 2275 PAPILLOM?  
 40380 VIRUS?  
 158 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 573 HPV  
 102 HPV16  
 35 HPV18  
 L24 711 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'USPATFULL'

134902 HUMAN?  
 766 PAPILLOM?  
 14071 VIRUS?  
 131 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 128 HPV  
 15 HPV16  
 9 HPV18  
 L25 207 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'INPADOC'

23155 HUMAN?  
 464 PAPILLOM?  
 10126 VIRUS?  
 90 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 58 HPV  
 1 HPV16  
 0 HPV18  
 L26 148 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'JAPIO'

17709 HUMAN?  
 36 PAPILLOM?  
 2268 VIRUS?  
 24 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 11 HPV  
 0 HPV16  
 0 HPV18  
 L27 31 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PAPERCHEM2'

1667 HUMAN?  
 0 PAPILLOM?  
 110 VIRUS?  
 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 4 HPV  
 0 HPV16  
 0 HPV18  
 L28 4 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PATDD'

558 HUMAN?  
 1 PAPILLOM?  
 190 VIRUS?  
 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 0 HPV  
 0 HPV16  
 0 HPV18  
 L29 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PATDPA'

970 HUMAN?  
 77 PAPILLOM?  
 1548 VIRUS?  
 1 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 16 HPV  
 1 HPV16  
 1 HPV18  
 L30 17 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PATOSDE'

567 HUMAN?  
 14 PAPILLOM?  
 383 VIRUS?  
 0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?  
 7 HPV  
 2 HPV16  
 2 HPV18  
 L31 9 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18



```

FILE 'PATOSEP'
6548 HUMAN?
73 PAPILLOM?
1877 VIRUS?
20 HUMAN? (5A) PAPILLOM? (5A) VIRUS?
32 HPV
5 HPV16
3 HPV18
L32 42 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PATOSWO'
4980 HUMAN?
59 PAPILLOM?
1583 VIRUS?
10 HUMAN? (5A) PAPILLOM? (5A) VIRUS?
22 HPV
4 HPV16
2 HPV18
L33 25 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'PIRA'
2253 HUMAN?
0 PAPILLOM?
179 VIRUS?
0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?
22 HPV
0 HPV16
0 HPV18
L34 22 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'RAPRA'
1058 HUMAN?
2 PAPILLOM?
49 VIRUS?
0 HUMAN? (5A) PAPILLOM? (5A) VIRUS?
4 HPV
0 HPV16
0 HPV18
L35 4 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

FILE 'WPIDS'
51006 HUMAN?
359 PAPILLOM?
13812 VIRUS?
133 HUMAN? (5A) PAPILLOM? (5A) VIRUS?
97 HPV
15 HPV16
7 HPV18
L36 166 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

TOTAL FOR ALL FILES
L37 30175 HUMAN? (5A) PAPILLOM? (5A) VIRUS? OR HPV OR HPV16 OR HPV18

=> s major (5a) histocompatibility (5a) complex? (5a) class (5a) i (5a) molecule? or MHC

TOTAL FOR ALL FILES
L74 86145 MAJOR (5A) HISTOCOMPATIBILITY (5A) COMPLEX? (5A) CLASS (5A)
) I (5A) MOLECULE? OR MHC

=> s l37 and l74

TOTAL FOR ALL FILES
L111 187 L37 AND L74

=> s l111 and (E6 or E7)

'E6' NOT FOUND
The E# entered is not currently defined.

=> s l111 and e6

'E6' NOT FOUND
The E# entered is not currently defined.

=> dup rem

ENTER L# LIST OR (END): l111

DUPLICATE IS NOT AVAILABLE IN 'DRUGLAUNCH'. ANSWERS FROM THESE FILES WILL BE
CONSIDERED UNIQUE
PROCESSING IS APPROXIMATELY 96% COMPLETE FOR L111

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PROCESSING COMPLETED FOR L111  
L112 66 DUP REM L111 (121 DUPLICATES REMOVED)

=> d bib ab 1-66

L112 ANSWER 1 OF 66 DRUGNL COPYRIGHT 1995 IMSWORLD

AN 95:118 DRUGNL  
TI Update on Viagene  
SO R&D Focus Drug News (6 Feb 1995).  
WC 896

L112 ANSWER 2 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:426198 NLDB  
TI Drug Development/Cancer Vaccines "Development of Vaccine and Immunotherapeutic Strategies for \*\*\*HPV\*\*\* Related Cervical Carcinoma." T.-C. Wu and D.M. Pardoll. Johns Hopkins Medical Institutions, Baltimore, Maryland.  
SO Vaccine Weekly, (16 Jan 1995) .  
ISSN: 1074-2921.  
PB Charles W Henderson  
DT Newsletter  
LA English  
WC 416

L112 ANSWER 3 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:514418 NLDB  
TI Disease Associations Possible Association Between Certain HLA Class II Haplotypes and Cervical Cancer  
SO Cancer Biotechnology Weekly, (27 Mar 1995) .  
PB CW Henderson, Publisher  
DT Newsletter  
LA English  
WC 962

L112 ANSWER 4 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:513920 NLDB  
TI Human Papillomavirus Peptide Engineering Allows Vaccination Against \*\*\*HPV\*\*\*  
SO Vaccine Weekly, (27 Mar 1995) .  
ISSN: 1074-2921.  
PB Charles W Henderson  
DT Newsletter  
LA English  
WC 453

L112 ANSWER 5 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 95:23020 NLDB  
TI Cytel Emphasizes New Targets  
SO Applied Genetics News, (Jun 1995) Vol. 15, No. 10.  
ISSN: 0271-7107.  
PB Business Communications Company, Inc  
DT Newsletter  
LA English  
WC 323

L112 ANSWER 6 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1995:442210 CAPLUS  
DN 122:211608  
TI Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein  
AU Wucherpfennig, Kai W.; Strominger, Jack L.  
CS Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA  
SO Cell (Cambridge, Mass.) (1995), 80(5), 695-705  
CODEN: CELLS5; ISSN: 0092-8674  
DT Journal  
LA English  
AB Structural similarity between viral T cell epitopes and self-peptides could lead to the induction of an autoaggressive T cell response. Based on the structural requirements for both \*\*\*MHC\*\*\* class II binding and TCR recognition of an immunodominant myelin basic protein (MBP) peptide, criteria for a data search were developed in which the degeneracy of amino acid side chains required for \*\*\*MHC\*\*\* class II binding and the conservation of those required for T cell activation were



considered. A panel of 129 peptides that matched the mol. mimicry motif was tested on seven MBP-specific T cell clones from multiple sclerosis patients. Seven viral and one bacterial peptide efficiently activated three of these clones. Only one peptide could have been identified as a mol. mimic by sequence alignment. The observation that a single T cell receptor can recognize quite distinct but structurally related peptides from multiple pathogens has important implications for understanding the pathogenesis of autoimmunity.

L112 ANSWER 7 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 1  
AN 95:157688 BIOSIS  
DN 98171988

TI Peptide engineering allows cytotoxic T-cell vaccination against  
\*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* tumour antigen, E6.

AU Lipford G B; Bauer S; Wagner H; Heeg K

CS Inst. Med. Microbiol., Tech. Univ. Munich, Trogerstr. 9, Munich  
81675, Germany

SO Immunology 84 (2). 1995. 298-303. ISSN: 0019-2805

LA English

AB Major histocompatibility complex ( \*\*\*MHC\*\*\* ) class I allele-specific binding motifs have proved useful in predicting cytotoxic T-cell epitopes from immunogenic proteins. In a search of the E6 protein from \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* type 16 utilizing the K-b binding motif, we discovered four potential binding peptides. One peptide, E6.1 (sequence 50-57, YDFAFRDL), was poor in its ability to stabilize empty K-b on RMA-S cells, with a  $t_{1/2}$  = 33 min versus 30 min for empty K-b. This peptide subsequently proved to be non-immunogenic upon mouse in vivo vaccination. It was hypothesized that an isoleucine for aspartate substitution at position 2 would improve K-b stabilization kinetics and therefore immunogenic potential. The engineered peptide E6.1 I2 increased the K-b  $t_{1/2}$  to 100 min and was immunogenic upon in vivo vaccination. Cytolytic T lymphocytes (CTL) raised with the E6.1 I2 peptide responded to cells pulsed with either the wild-type peptide or the engineered peptide, implying a blindness to the substitution. More striking, these CTL also lysed a syngeneic cell line transfected with the E6 gene, implying that the E6.1 peptide was processed and presented. These data demonstrate that subimmunogenic peptides can be engineered to improve binding kinetics, which in turn improves immunogenicity. Provided that poor binding peptides are processed, the induction threshold for CTL activation can be achieved with engineered peptides, thus allowing for the kill of wild-type target cells. This approach may prove relevant to the design of subunit vaccines to vitally induced tumours.

L112 ANSWER 8 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 2  
AN 95:190328 BIOSIS  
DN 98204628

TI Expression of \*\*\*HPV\*\*\* -16 E5 protein in keratinocytes leads to post-transcriptional loss of \*\*\*MHC\*\*\* -1 and TAP-1.

AU McCance D J; Cromme F V; Straight S W; Tsao G; Pleogh H L; Meijer C J L M; Walboomers J M M

CS Dep. Microbiol. Immunol., Univ. Rochester, Rochester, NY 14662, USA

SO Keystone Symposium on Molecular Aspects of Viral Immunity, Keystone, Colorado, USA, January 16-23, 1995. Journal of Cellular Biochemistry Supplement 0 (19A). 1995. 292. ISSN: 0733-1959

DT Conference

LA English

L112 ANSWER 9 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 3  
AN 95:73675 BIOSIS  
DN 98087975

TI Ultrastructural localization of stem cell factor in canine marrow-derived stromal cells.

AU Huss R; Hong D-S; Beckham C; Kimball L; Myerson D H; Storb R; Deeg H J

CS Fred Hutchinson Cancer Res. Cent., 1124 Columbia Street, M318, Seattle, WA 98104-2092, USA

SO Experimental Hematology (Charlottesville) 23 (1). 1995. 33-40. ISSN: 0301-472X

LA English

AB Stromal cell lines derived from canine long-term bone marrow cultures (LTBMC) were characterized regarding the expression of growth factors and especially the localization of stem cell factor (SCF) (c-kit ligand). One cell line (DO64) was immortalized by transformation with a retroviral vector containing the open reading frames (ORFs) E6 and E7 of the \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* type 16 ( \*\*\*HPV\*\*\* -16). Transfection did not change cellular characteristics but rendered the cell line more independent from culture conditions. The transformed line DO64 consisted mainly of



fibroblast-like cells. In addition, some cells showed endothelial and some smooth-muscle cell features. Stromal cells expressed a broad spectrum of surface markers, including low levels of major histocompatibility-complex ( \*\*\*MHC\*\*\* ) class-II antigens. A new murine monoclonal antibody (MAb), RG7.6 (IgG1), specific for canine SCF, recognized the majority of fibroblast-like stromal cells. The staining pattern for SCF showed perinuclear and intracytoplasmic dense areas. Immunoelectron microscopy revealed the localization of SCF in secretory vesicles, the perivesicular cytoplasm, and bound to the cytoplasmic membrane. RNA analysis showed that stromal cells transcribed, in addition to SCF, messages for granulocyte colony-stimulating factor (G-CSF), granulocyte-monocyte CSF (GM-CSF), interleukin-6 (IL-6), and transforming growth factor-beta (TGF-beta). In summary, we have established and characterized canine marrow-derived stromal cell lines, and using the new MAb RG7.6, we have localized SCF to cytoplasmic vesicles as well as the membrane of stromal cells.

L112 ANSWER 10 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:389594 NLDB  
 TI Biotechnology - Vaccine Engineering: "New Strategies in Vaccine Engineering." D.M. Pardoll. Johns Hopkins University School of Medicine.  
 SO Vaccine Weekly, (5 Dec 1994) .  
 ISSN: 1074-2921.  
 PB Charles W Henderson  
 DT Newsletter  
 LA English  
 WC 795

L112 ANSWER 11 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:44272 NLDB  
 TI Encouraging Developments  
 SO Antiviral Agents Bulletin, (Jan 1994) Vol. 7, No. 1.  
 ISSN: 0897-9871.  
 PB Biotechnology Information Institute  
 DT Newsletter  
 LA English  
 WC 2661

L112 ANSWER 12 OF 66 COPYRIGHT 1995 PJB

AN 94:17778 PHIN  
 DN S00420996  
 DED 22 Nov 1994  
 TI British Technology Group (BTG) seeks new development capital  
 SO Scrip (1994) No. 1977 p16  
 DT Newsletter  
 FS FULL

L112 ANSWER 13 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1994:455887 CAPLUS  
 DN 121:55887  
 TI Antigenic peptides binding class I \*\*\*MHC\*\*\* proteins and their diagnostic and therapeutic uses  
 IN Kubo, Ralph T.; Grey, Howard M.; Sette, Alessandro; Celis, Esteban  
 PA Cytel Corp., USA  
 SO PCT Int. Appl., 149 pp.  
 CODEN: PIXXD2  
 PI WO 9403205 A1 940217  
 DS W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN  
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
 AI WO 93-US7421 930806  
 PRAI US 92-926666 920807  
 US 93-27746 930305  
 DT Patent  
 LA English  
 AB Antigenic peptides capable of specifically binding selected \*\*\*MHC\*\*\* antigens and inducing T cell activation in T cells restricted by the corresponding \*\*\*MHC\*\*\* allele are described. The peptides are used to elicit an immune response against a desired antigen. HLA-A antigens were purified by affinity chromatog. against allele-specific or monoclonal antibodies. Peptides remaining bound to the HLA-A antigens after affinity purifn. were eluted at acidic pH, fractionated by HPLC and individual fractions immobilized and sequenced. Residues essential for binding to the



antigen were detected during sequencing were obsd. in complex fractions by being the major amino acid in a given cycle of the sequencing reaction. A decapeptide specific for an HLA-A3.2 antigen was obsd. with position 2 V, L; or M, position 3 Y or D; position 7 I; position 8 Q or N; and positions 9 and 10 both K. Similarly, motifs were obsd. for HLA-A1, A11, and A24.1. Antigens contg. these motifs were searched for in sequence databases and a no. of such sequences were found in tumor-specific antigens and viral proteins. These peptides were used as probes for the assay of the cognate HLA-A antigens.

L112 ANSWER 14 OF 66 WPIDS COPYRIGHT 1995 DERWENT INFORMATION LTD

AN 94-035970 [05] WPIDS

DNC C94-016558

TI Monoclonal antibodies for diagnosis or therapy - directed against conjugate of \*\*\*MHC\*\*\* class I mol and peptide antigen.

DC B04 D16

IN HAEMMERLING, G

PA (DEKR-N) DEUT KREBSFORSCHUNGSZENTRUM

CYC 1

PI DE 4224542 A1 940127 (9405)\* 3 pp

ADT DE 4224542 A1 DE 92-4224542 920724

PRAI DE 92-4224542 920724

AB DE 4224542 A UPAB: 940315

Producing monoclonal antibodies directed against a conjugate of a major histocompatibility complex class I mol. (I) and a peptide antigen (II) comprises (a) isolating (I); (b) inserting a (I)-encoding gene into the genome of a mouse to permit expression of the gene; (c) conjugating (I) with (II); (d) immunising the transformed mouse with the conjugate; (e) isolating spleen cells from the mouse; and (f) producing and opt. humanising monoclonal antibodies in known manner.

Process (I) may be isolated from CS7 AL/6 mouse RMA-S tumour cells or human EBV transformed cells, or may be isolated from tissue, or may be produced by recombinant DNA techniques. Step (b) may be omitted if (I) was isolated from the same mouse strain as that to be immunised. (II) may be a viral or tumour antigen, e.g. the human melanoma antigen MAGE-1 or the tumour antigen produced by the \*\*\*HPV\*\*\* E6 or E7 oncogene.

USE - The antibodies are useful for diagnosis and therapy of tumours and infections, e.g. as a substitute for tumour-specific cytotoxic T cells.  
Dwg.0/0

L112 ANSWER 15 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 95:1473 BIOSIS

DN 98015773

TI \*\*\*HPV\*\*\* 16-derived synthetic peptides with ability to upregulate \*\*\*MHC\*\*\* class I expression on RMA-S or T2 cells, as detected by enzyme immunoassay.

AU Diltner J

CS Dep. Virology, Karolinska Inst., Stockholm, Sweden

SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second International Workshop on HPV Immunology, Cambridge, England, UK, July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA; London, England, UK. 0 (0). 1994. 201-205. ISBN: 0-306-44714-2

DT Book; Conference

LA English

L112 ANSWER 16 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 95:1470 BIOSIS

DN 98015770

TI Analysis of \*\*\*MHC\*\*\* class I expression in \*\*\*HPV\*\*\* 16 positive cervical carcinomas, in relation to c-myc overexpression.

AU Cromme F V; Snijders P J F; Van Den Brule A J C; Stukart M J; Kenemans P; Meijer C J L M; Walboomers J M

CS Dep. Pathology, Section Molecular Pathology, Free Univ. Hosp., De Boelelaan 1117, 1081 HV Amsterdam, Netherlands

SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second International Workshop on HPV Immunology, Cambridge, England, UK, July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA; London, England, UK. 0 (0). 1994. 181-188. ISBN: 0-306-44714-2

DT Book; Conference

LA English

L112 ANSWER 17 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 95:1472 BIOSIS

DN 98015772

TI Recurrent respiratory papillomatosis (RRP): Enriched HLA DQw3 phenotype and decreased class I \*\*\*MHC\*\*\* expression.

AU Bonagura V R; O'Reilly M E; Abramson A L; Steinberg B M



CS Dep. Pediatrics, Long Island Jewish Med. Cent., New Hyde Park, NY  
11042, USA

SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second  
International Workshop on HPV Immunology, Cambridge, England, UK,  
July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA;  
London, England, UK. 0 (0). 1994. 195-200. ISBN: 0-306-44714-2

DT Book; Conference

LA English

L112 ANSWER 18 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 95:1474 BIOSIS

DN 98015774

TI Regulation of \*\*\*MHC\*\*\* class I, class II and ICAM-1 expression  
by cytokines and retinoids in \*\*\*HPV\*\*\* -harboring keratinocyte  
lines.

AU Majewski S; Breitburd F; Orth G; Jablonska S

CS Dep. Dermatology, Warsaw Sch. Med., Kszykowa 82a, 02-008 Warsaw,  
Poland

SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second  
International Workshop on HPV Immunology, Cambridge, England, UK,  
July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA;  
London, England, UK. 0 (0). 1994. 207-211. ISBN: 0-306-44714-2

DT Book; Conference

LA English

L112 ANSWER 19 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 95:1469 BIOSIS

DN 98015769

TI Major histocompatibility complex ( \*\*\*MHC\*\*\* ) expression and  
antigen presentation in cervical cancer.

AU Bartholomew J S; Stacey S N; Coles B; Duggan-Keen M; Dyer P A; Glew S  
S; Keating P J; Arrand J R; Stern P L

CS Cancer Res. Campaign, Dep. Immunology, Paterson Inst. Cancer Res.,  
Christie Hosp. NHS Trust, Manchester, UK

SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second  
International Workshop on HPV Immunology, Cambridge, England, UK,  
July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA;  
London, England, UK. 0 (0). 1994. 173-179. ISBN: 0-306-44714-2

DT Book; Conference

LA English

L112 ANSWER 20 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1995:8346 CAPLUS

DN 122:7346

TI Role of HLA-A motifs in identification of potential CTL epitopes in  
human papillomavirus type 16 E6 and E7 proteins

AU Kast, W. Martin; Brandt, Remco M. P.; Sidney, John; Drijfhout, Jan  
Wouter; Kubo, Ralph T.; Grey, Howard M.; Melief, Cornelis J. M.;  
Sette, Alessandro

CS Dep. Immunohematol., Univ. Hosp., Leiden, Neth.

SO J. Immunol. (1994), 152(8), 3904-12

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The authors have measured the binding affinity for five HLA-A  
alleles: HLA-A1 (A\*0101), A2.1 (A\*0201), A3 (A\*0301), A11 (A\*1101),  
and A24 (A\*2401); of a set of all possible nonamer peptides of human  
papillomavirus type 16 E6 and E7 proteins. High affinity binding  
peptides were identified for each of the alleles, thus allowing the  
authors to select several candidates for CTL-based vaccines.  
Moreover, this unbiased set of peptides allowed an evaln. of the  
predictive value of HLA motifs derived either from the anal. of  
sequencing of pools of naturally processed peptides or from the  
binding anal. of polyaniline nonameric peptides that differed in the  
amino acids (aa) present at the anchor positions. Whereas pool  
sequence-derived motifs were present in only 27% of high affinity  
binders, the more expanded motif, based on anal. of different aa  
substitutions at the anchor positions, was present in 73% of high  
affinity binders. Furthermore, it was found that the presence of  
anchor residues in a peptide was in itself not sufficient to det.  
binding to \*\*\*MHC\*\*\* class I mols., because the majority of  
motif-contg. peptides failed to bind to the relevant \*\*\*MHC\*\*\*.  
Finally, specific HLA motifs were used to predict peptide binders of  
8, 10, and 11 aa in length. Several high affinity binding peptides  
were identified for each of the various peptide lengths, indicating  
a significant size heterogeneity in peptides capable of high  
affinity binding to HLA-A mols.

L112 ANSWER 21 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 4

AN 95:80678 BIOSIS

DN 98094978



TI Identification of a naturally processed HLA A0201-restricted viral peptide from cells expressing human papillomavirus type 16 E6 oncoprotein.

AU Bartholomew J S; Stacey S N; Coles B; Burt D J; Arrand J R; Stern P L  
CS Dep. Immunol., Cancer Res. Campaign Lab., Paterson Inst. Cancer Res.,  
Christie Hosp. NHS Trust, Wilmslow Road, Manchester M20 9BX, UK  
SO European Journal of Immunology 24 (12). 1994. 3175-3179. ISSN:  
0014-2980

LA English

AB Human papillomavirus (HPV) DNA encoding the oncogenic proteins E6 and E7 is usually retained in cervical carcinomas, implicating these proteins as potential target antigens for immune recognition in this virally associated tumor. We have characterized endogenously processed peptides eluted from \*\*\*major\*\*\*  
\*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\*  
\*\*\*I\*\*\* \*\*\*molecules\*\*\* in cells infected with a recombinant vaccinia expressing the \*\*\*HPV\*\*\* -16 E6 oncoprotein. The reverse-phase chromatography profile of peptides eluted from isolated HLA-A0201 molecules in cells expressing the E6 oncoprotein differs from that of cells not expressing E6. Sequential Edman degradation of novel peaks found in the peptide profiles from cells expressing \*\*\*HPV\*\*\* -16 E6 led to the identification of a naturally processed HLA-A0201-restricted E6 peptide of sequence KLPQLCTEL. This approach has allowed the identification of a viral peptide which is processed and presented by cells expressing the E6 oncoprotein and is a likely target for cytotoxic T lymphocyte recognition in HLA-A0201-positive patients.

L112 ANSWER 22 OF 66 CANCERLIT DUPLICATE 5

AN 95093344 CANCERLIT

TI DQA1 and DQB1 genes in patients with squamous cell carcinoma of the cervix: relationship to human papillomavirus infection and prognosis.

AU Helland A; Biresen A L; Kristensen G; Rnningen K S  
CS Department of Genetics, Norwegian Radium Hospital, Oslo.  
SO Cancer Epidemiol Biomarkers Prev. (1994). Vol. 3, No. 6, pp. 479-86.  
Journal code: BNJ. ISSN: 1055-9965.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; L; Priority Journals

LA English

OS MEDLINE 95093344

EM 9502

AB Women carrying serological HLA-DQ3 specificity have previously been found to have an increased risk of developing squamous cell carcinoma of the cervix. Here we report the distribution of DQA1 and DQB1 genes in 158 Norwegian patients with squamous cell carcinoma of the cervix and in 186 ethnically matched controls. The DQA1 typing revealed an increase of the DQA1\*030X allele among the patients compared to the controls [odds ratio (OR) = 1.77] and a decreased frequency of DQA1\*0201 among the patients (OR = 0.57). DQB1\*0301 was increased (OR = 1.81) and DQB1\*0201 was decreased (OR = 0.64) among the patients compared to the controls. Among the patients, 67% carried genes encoding DQ3 (DQB1\*0301, DQB1\*0302, or DQB1\*0303) compared to 51% of the controls, which gives an odds ratio of 2.0, significant both in corrected and uncorrected statistical analysis. The haplotype DQA1\*0201-DQB1\*0201 was decreased among the patients compared to the controls (OR = 0.38). Human papillomavirus (\*\*\*HPV\*\*\* ) has been demonstrated to be a contributing factor in the development of this carcinoma. Primary tumors (fresh frozen) from 65 of the patients were analyzed for the presence of \*\*\*HPV\*\*\* 16 and \*\*\*HPV\*\*\* 18 by polymerase chain reaction. The DQA1-DQB1 haplotypes were distributed randomly among the patients with \*\*\*HPV\*\*\* 16 or \*\*\*HPV\*\*\* 18 present in their tumors so no association was found. Neither was there any difference between DQ3-positive and DQ3-negative patients in the frequency of \*\*\*HPV\*\*\* 16- or \*\*\*HPV\*\*\* 18-positive tumors. DQB1\*03 showed no independent significant association with relapse-free survival.(ABSTRACT TRUNCATED AT 250 WORDS)

L112 ANSWER 23 OF 66 SCISEARCH COPYRIGHT 1995 ISI (R)

AN 94:676087 SCISEARCH

GA The Genuine Article (R) Number: PM446

TI HUMAN PAPILLOMAVIRUSES

AU ZURHAUSEN H (Reprint); DEVILLIERS E M

CS DEUTSCH KREBSFORSCHUNGSZENTRUM, NEUENHEIMER FELD 280, D-69120  
HEIDELBERG, GERMANY (Reprint)

CYA GERMANY

SO ANNUAL REVIEW OF MICROBIOLOGY, (1994) Vol. 48, pp. 427-447.  
ISSN: 0066-4227.

DT General Review, Journal

FS LIFE



LA ENGLISH

REC Reference Count 123

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB During the past 17 years 73 genotypes of human pathogenic papillomaviruses ( \*\*\*HPV\*\*\* ) have been identified. Most of them are found in benign proliferations; however, several have been discovered in malignant tumors. Specifically, cancer of the cervix, other anogenital cancers, but also some cancers of the skin, the oral and nasal cavity, and the rare periungual carcinomas have been linked to specific \*\*\*HPV\*\*\* infections. The pathogenesis of cancer of the cervix has been particularly well studied. Specific viral genes (E6 and E7) of high risk HPVs (types 16, 18, and others) act as oncogenes. Their expression emerges as necessary but not sufficient factors for malignant conversion. Besides stimulating cell proliferation, they are responsible for the genetic instability of the infected cells. Their transcriptional and functional activity is regulated by host cell genes. Mutational modifications of the latter appear to be required for malignant progression.

L112 ANSWER 24 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1994:628574 CAPLUS

DN 121:228574

TI T-cell epitope mapping in human papillomavirus type 16 E6 oncoprotein

AU Gao, Liqun; Chain, Benjamin; Sinclair, Christine; Sadovnikova, Elena; Stauss, Hans, J.; Zhu, Xiaojie; Beverley, Peter C. L.; Crawford, Lionel

CS Dep. Biol., Univ. Coll. London, London, WC1E 6BT, UK

SO Vaccines 94: Mod. Approaches New Vaccines Incl. Prev. AIDS, [Annu. Meet.], 11th (1994), Meeting Date 1993, 333-8. Editor(s): Norrby, Erling. Publisher: Cold Spring Harbor Lab. Press, Cold Spring Harbor, N.Y.

CODEN: 60PMAJ

DT Conference

LA English

AB The authors used a murine model system to test the immunogenicity of a vaccinia construct, rVV16 E6/360, which can express \*\*\*HPV16\*\*\* -E6 protein in infected cells. This study illustrates the complexity of epitope generation in cytotoxic T-cell responses and suggests other factors, besides \*\*\*MHC\*\*\* binding, may play an important role in detg. the specificity of the immune response even to relatively simple protein antigens.

L112 ANSWER 25 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 6

AN 94:160183 BIOSIS

DN 97173183

TI Limitations of predictive motifs revealed by cytotoxic T lymphocyte epitope mapping of the \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* E7 protein.

AU Sadovnikova E; Zhu X; Collins S M; Zhou J; Vousden K; Crawford L; Beverley P; Stauss H J

CS ICRF Tumour Immunol. Unit, Univ. Coll. London Med. Sch., Courtauld Inst., 91 Riding House St., London W1P 8BT, UK

SO International Immunology 6 (2). 1994. 289-296. ISSN: 0953-8178

LA English

AB \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 16 is found in the majority of cervical cancer patients and the transforming protein E7 is consistently expressed in cancer cells, making it a potential target for immune attack. In this study we have investigated whether E7 gains access to the \*\*\*MHC\*\*\* class I processing pathway and provides cytotoxic T lymphocyte (CTL) stimulating peptide epitopes. CTL were induced in H-2-b mice by immunization with recombinant vaccinia virus expressing E7 (Vac-E7). To map CTL recognition, natural peptides were purified from cells expressing either intact or truncated E7 protein. Following peptide separation by HPLC one major CTL epitope was detected and truncated constructs localized this epitope to the C-terminal region. Mapping with synthetic peptides indicated that residues 49 - 57 (RAHYNIVTF) were recognised by anti-E7 CTL. Synthetic 49 - 57 peptide was used to induce CTL, which recognized the same HPLC purified natural peptide fractions as anti-E7 CTL. Binding motifs for H-2-b class I molecules did not predict residues 49 - 57 to be a CTL epitope, but instead the sequence 21 - 28 (DLYCYEQL) which contains a Kb anchor motif. Synthetic 21 - 28 peptide was found to bind to K-b Class I molecules and readily induced CTL, indicating that the T cell repertoire of H-2-b mice can recognize this epitope. However, these CTL did not recognize peptides isolated from E7 expressing cells, showing that natural processing did not produce detectable levels of the 21 - 28 epitope. Together, the data demonstrate that an unexpected E7 peptide can function as a major CTL epitope.



L112 ANSWER 26 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 7

AN 94:226091 BIOSIS

DN 97239091

TI Enzyme immunoassay detection of induction of \*\*\*MHC\*\*\* class I expression by synthetic peptides from the E6 and E7 regions of human papillomavirus type 16.

AU Dillner J

CS Dep. Virol., Karolinska Inst., SBL, S-10521 Stockholm, SWE

SO Journal of Immunological Methods 167 (1-2). 1994. 195-205. ISSN: 0022-1759

LA English

AB Viral antigens are presented to cytotoxic T cells (CTL) in the form of endogenously processed peptides bound to \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* ( \*\*\*MHC\*\*\* ) \*\*\*class\*\*\* \*\*\*molecules\*\*\*. A variety of different methods for measuring the ability of peptides to bind to \*\*\*MHC\*\*\* class I have been described. Several of these methods use the murine lymphoma mutant cell line RMA-S, which has a peptide loading defect resulting in a low expression of surface class I molecules that can be upregulated if a synthetic binding peptide with class I binding ability is added to the culture medium. In order to be able to screen for peptides with \*\*\*MHC\*\*\* class I binding ability, we developed an enzyme immunoassay for quantitation of \*\*\*MHC\*\*\* class I expression on RMA-S cells. 107 synthetic peptides derived from the E6 and E7 regions of human papillomavirus type 16 were screened for ability to upregulate class I expression of K-b or D-b alleles. At a concentration of about 300 mu-M, 8/107 peptides were found to restore expression of D-b to equal or greater levels than found in the RMA-S parental cell line RMA, while 35/107 peptides were able to partially restore D-b expression. For K-b, 16/107 peptides were able to restore expression and 40/107 peptides induced partial upregulation. Titration experiments showed that upregulation of class I expression by these peptides was dependent on a high peptide concentration, since consistent upregulation could in no case be detected at concentrations below 10 mu-M. The class I binding peptides identified in the present study may be useful in the study of the CTL response to \*\*\*HPV\*\*\* in mouse model systems. The enzyme immunoassay used could facilitate the rapid search for class I binding peptides.

L112 ANSWER 27 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 94:405996 BIOSIS

DN 97418996

TI T cell epitopes in \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* proteins.

AU Sadovnikova E; Stauss H J

CS Imperial Cancer Res. Fund, Tumour Immunol. Group, Univ. Coll. London Med. Sch., Courtauld Inst., 91 Riding House St., London W1P 8BT, UK

SO Behring Institute Mitteilungen 0 (94). 1994. 87-93. ISSN: 0301-0457

LA English

AB Infection by \*\*\*HPV\*\*\* is associated with several human diseases such as warts of the skin, condylomata of the genital track and carcinoma of the cervix. Although there is strong evidence for immune control of \*\*\*HPV\*\*\* types causing warts and condylomata, it is currently unclear whether patients infected with transforming \*\*\*HPV\*\*\* types can mount efficient T cell responses. Despite the apparent low immunogenicity of transforming \*\*\*HPV\*\*\* types, several T-h and CTL epitopes have been identified in proteins derived from \*\*\*HPV16\*\*\*. This transforming virus is most frequently present in women with CIN and cervical carcinoma and knowledge of T cell recognisable proteins may eventually lead to the design of immune-stimulating anti- \*\*\*HPV16\*\*\* vaccines.

L112 ANSWER 28 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 8

AN 94:406226 BIOSIS

DN 97419226

TI Class I \*\*\*MHC\*\*\* -peptide interaction: Structural and functional aspects.

AU Ruppert J; Kubo R T; Sidney J; Grey H M; Sette A

CS Cytel, 3525 John Hopkins Court, San Diego, CA 92121, USA

SO Behring Institute Mitteilungen 0 (94). 1994. 48-60. ISSN: 0301-0457

LA English

AB The structural requirements for the interaction between antigens and class I molecules was investigated through the use of a quantitative assay to measure peptide binding to different \*\*\*MHC\*\*\* class I alleles. We determined the permissiveness of the main anchors reported by Rammensee and his group for peptide binding and defined an extended motif for peptides binding to the HLA-A2.1 allele, including the role of non-anchor positions. It was found that the main anchors were necessary, but not sufficient, for good binding. Certain non-anchor positions contributed significantly to overall binding and were referred to as secondary anchors. This finding



allowed a better prediction of high affinity binding peptides selected from libraries of different viral and tumor proteins. Furthermore, our data allowed correlation of the structural requirements for binding of peptides with crystallographic data of the \*\*\*MHC\*\*\* molecule. In order to characterize allele-specific motifs for a larger number of alleles, the HLA-A alleles A1, A3, A11, and A24, which represent some of the most common alleles found in different ethnic populations, were chosen. Here, most motifs were found to be highly exclusive; however, HLA-A3 and A11 shared a common motif. The defined motifs were validated further by using naturally processed peptides. Those peptides were also synthesized and tested for binding to the appropriate HLA alleles, giving a binding affinity from 0.3 to 200 nM for sequences of naturally processed peptides. Finally, a set of all possible 9-mer peptides from \*\*\*HPV\*\*\* 16 proteins were synthesized and tested for binding to the five class I alleles. For each allele, high affinity binders were identified, thus allowing for selection of possible peptide candidates for a CTL based vaccine.

L112 ANSWER 29 OF 66 DRUGNL COPYRIGHT 1995 IMSWORLD

AN 93:953 DRUGNL  
 TI Phase I For TA- \*\*\*HPV\*\*\*  
 SO R&D Focus Drug News (27 Sep 1993).  
 WC 164

L112 ANSWER 30 OF 66 DRUGNL COPYRIGHT 1995 IMSWORLD

AN 93:466 DRUGNL  
 TI Cantab Pipeline  
 SO R&D Focus Drug News (17 May 1993).  
 WC 1061

L112 ANSWER 31 OF 66 DRUGNL COPYRIGHT 1995 IMSWORLD

AN 93:659 DRUGNL  
 TI Viagene Pipeline  
 SO R&D Focus Drug News (19 Jul 1993).  
 WC 1065

L112 ANSWER 32 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:151455 NLDB  
 TI Peptide Vaccination with a Cytotoxic T-Cell Epitope Derived from the \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\* \*\*\*Virus\*\*\* Type 16 Oncogene E7 Confers Protection Against \*\*\*HPV16\*\*\* -Induced Tumors  
 SO Cancer Weekly, (26 Apr 1993) .  
 ISSN: 0896-7384.  
 PB CW Henderson, Publisher  
 DT Newsletter  
 LA English  
 WC 359

L112 ANSWER 33 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:134063 NLDB  
 TI Protection Against a \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\* \*\*\*Virus\*\*\* Type 16 -Induced Tumor by Peptide Vaccination with a Cytotoxic T -Cell Epitope Derived from the Viral Oncogene E7  
 SO Cancer Weekly, (19 Apr 1993) .  
 ISSN: 0896-7384.  
 PB CW Henderson, Publisher  
 DT Newsletter  
 LA English  
 WC 296

L112 ANSWER 34 OF 66 CAPLUS COPYRIGHT 1995 ACS DUPLICATE 9

AN 1994:426884 CAPLUS  
 DN 121:26884  
 TI Peptides of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* for use in \*\*\*human\*\*\* T cell response-inducing compositions  
 IN Kast, Wybe Martin; Melief, Cornelis Joseph Maria; Sette, Alessandro D.; Sidney, John C.  
 PA Rijksuniversiteit Leiden, Neth.  
 SO PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 PI WO 9322338 A1 931111  
 DS W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN  
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR,



IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
AI WO 93-NL93 930504  
PRAI EP 92-201252 920505  
EP 92-203870 921210  
EP 93-200243 930201  
EP 93-200621 930305  
DT Patent  
LA English  
AB A peptide comprising an amino acid sequence derived from a  
\*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* )  
protein, wherein said amino acid sequence has the ability to bind to  
a human Major Histocompatibility Complex Class I mol., is claimed.  
The peptides may be used in prophylactic or therapeutic treatment of  
cervical carcinoma and other \*\*\*HPV\*\*\* -related diseases (no  
data). Nine-residue peptides derived from \*\*\*HPV16\*\*\* or  
\*\*\*HPV18\*\*\* E6 and E7 proteins which bound to HLA-A2.1, -A1,  
-A2.1, -A3.2, -A11.2, and -A24 mols. were identified.

L112 ANSWER 35 OF 66 CAPLUS COPYRIGHT 1995 ACS DUPLICATE 10  
AN 1993:546568 CAPLUS  
DN 119:146568  
TI Nontoxic lipid vaccine formulations  
IN Barchfeld, Gail L.; Ott, Gary; Ralston, Robert; Selby, Mark; Spaete,  
Richard; Van Nest, Gary; Walker, Christopher  
PA Chiron Corp., USA  
SO PCT Int. Appl., 32 pp.  
CODEN: PIXXD2  
PI WO 9314744 A1 930805  
DS W: AU, CA, JP  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
AI WO 93-US1102 930204  
PRAI US 92-830612 920204  
US 92-885905 920518  
US 92-942639 920909  
DT Patent  
LA English  
OS MARPAT 119:146568  
AB A vaccine formulation for inducing class I \*\*\*MHC\*\*\* -restricted  
T cell immunity comprises (1) an effective amt. of an immunogenic  
antigen and (2) a lipid suspension comprising a cell  
membrane-fusible pos.-charged lipid in aggregation with the antigen.  
The lipid suspensions are capable of delivering antigens directly to  
the cytoplasm of host cells, bypassing the normal endocytic pathway.  
The ability of N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium  
methylsulfate to deliver recombinant gB2 to target cells for  
recognition by HSV-specific cytotoxic T lymphocytes was assessed.

L112 ANSWER 36 OF 66 USPATFULL  
AN 93:89648 USPATFULL  
TI Covalent polar lipid-peptide conjugates for immunological  
targeting  
IN Yatvin, Milton B., Portland, OR, United States  
Stowell, Michael H. B., Pasadena, CA, United States  
Malkovsky, Miroslav, Madison, WI, United States  
PA State of Oregon, Portland, OR, United States (U.S. state  
government)  
PI US 5256641 931026  
AI US 92-911209 920709 (7)  
RLI Continuation-in-part of Ser. No. US 90-607982, filed on 1 Nov  
1990, now patented, Pat. No. US 5149794  
DT Utility  
EXNAM Primary Examiner: Rollins, John W.  
LREP Allegretti & Witcoff, Ltd.  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
GI 7 Drawing Figure(s); 8 Drawing Page(s)  
LN.CNT 676

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention relates to methods of facilitating the entry of  
peptides into cells and targeting such peptides to specific  
organelles within the cell. The invention provides methods for  
delivering and specific targeting of antigenically-active peptides  
to cells for the specific production of immunological reactivity  
against such peptides, as well as compositions and pharmaceutical  
compositions of matter comprising such peptides. This invention  
thereby provides improved methods for vaccine production and in  
vivo vaccination against pathogenic microorganisms. Methods for  
alleviating autoimmune disease and ameliorating tissue and organ  
transplant rejection using such conjugates are also provided.

L112 ANSWER 37 OF 66 USPATFULL



AN 93:84900 USPATFULL  
 TI Artificial viral envelopes  
 IN Schreier, Hans, Gainesville, FL, United States  
 Chander, Ramesh, Bombay, India  
 Stecenko, Arlene A., Gainesville, FL, United States  
 PA Univ. of Florida Research Foundation, Inc., Gainesville, FL,  
 United States (U.S. corporation)  
 PI US 5252348 931012  
 AI US 92-923016 920730 (7)  
 RLI Continuation of Ser. No. US 90-600641, filed on 19 Oct 1990, now  
 abandoned  
 DT Utility  
 EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Kishore,  
 G. S.  
 LREP Saliwanchik & Saliwanchik  
 CLMN Number of Claims: 5  
 ECL Exemplary Claim: 1  
 GI No Drawings  
 LN.CNT 731

AB The production of artificial viral envelopes by a novel  
 double-detergent dialysis technique is disclosed. Specifically  
 exemplified is the production of HIV-1 and RSV viral envelopes.  
 The resulting artificial viral envelopes are essentially identical  
 to the natural virus with regard to characteristics which are  
 relevant to immunogenicity.

L112 ANSWER 38 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 11

AN 94:20191 BIOSIS

DN 97033191

TI \*\*\*MHC\*\*\* class I expression in \*\*\*HPV\*\*\* 16 positive  
 cervical carcinomas is post-transcriptionally controlled and  
 independent from c-myc overexpression.

AU Cromme F V; Snijders P J F; Van Den Brule A J C; Kenemans P; Meijer C  
 J L M; Walboomers J M M

CS Inst. Pathol., Sect. Molecular Pathol., Free Univ. Hosp., De  
 Boelelaan 1117, 1018 HV Amsterdam, NET

SO Oncogene 8 (11). 1993. 2969-2975. ISSN: 0950-9232

LA English

AB Squamous cell carcinomas of the uterine cervix (n = 23) were selected  
 for the presence of human papillomavirus type 16 ( \*\*\*HPV\*\*\* 16)  
 using the polymerase chain reaction (PCR). Localization of  
 transcripts coding for the E7 protein was demonstrated in neoplastic  
 cells with RNA in situ hybridization. Consecutive tissue sections  
 were investigated for expression of the major histocompatibility  
 complex class I ( \*\*\*MHC\*\*\* -1) and c-myc using immunohistochemical  
 double staining procedures, since a role has been suggested for the  
 c-myc protein in \*\*\*MHC\*\*\* -1 down-regulation and c-myc  
 overexpression has been described in cervical carcinomas. Reduced  
 expression of class I heavy chains was observed in neoplastic cells  
 from 18 out of 23 carcinomas (78%). Varying levels of c-myc  
 overexpression were observed in 12 carcinomas (52%), from which four  
 showed positive \*\*\*MHC\*\*\* -1 expression in c-myc overexpressing  
 cells. In the remaining eight c-myc overexpressing carcinomas  
 \*\*\*MHC\*\*\* -1 down-regulation was observed. Additional RNA in situ  
 hybridization with class I heavy chain locus-specific RNA-probes  
 revealed presence of class I mRNAs in those neoplastic cells that  
 show negative staining for \*\*\*MHC\*\*\* -1 protein. These data  
 strongly indicate that \*\*\*MHC\*\*\* -1 down-regulation in cervical  
 carcinomas involves post-transcriptional mechanisms, not directly  
 related to E7 transcription and overexpression of c-myc.

L112 ANSWER 39 OF 66 CANCERLIT DUPLICATE 12

AN 93233248 CANCERLIT

TI Production and characterization of human proliferative T-cell clones  
 specific for human papillomavirus type 1 E4 protein.

AU Steele J C; Stankovic T; Gallimore P H

CS Department of Cancer Studies, Medical School, University of  
 Birmingham, United Kingdom.

SO J Virol, (1993). Vol. 67, No. 5, pp. 2799-806.

Journal code: KCV. ISSN: 0022-538X.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals

LA English

OS MEDLINE 93233248

EM 9306

AB Human papillomavirus type 1 (HPV1) virions and E4 protein purified  
 from cutaneous warts were tested in lymphocyte proliferation assays  
 using normal individuals. Both antigens were found to be capable of  
 eliciting good lymphoproliferative responses. Several T-cell clones  
 specific for wart E4 protein were obtained from a donor who had  
 consistently responded very well to E4 in these initial assays. They



were maintained in culture by repeated stimulation with antigen and interleukin-2, using an autologous mitomycin-treated lymphoblastoid cell line as a source of antigen-presenting cells. Two of these clones (3F5 and 4A8), which behaved identically, have been studied in more detail. A series of overlapping synthetic peptides covering the entire E1 E4 protein sequence was used to identify a single T-cell epitope which maps to a strongly hydrophilic region spanning amino acid residues 38 to 50. We have also tested the ability of a panel of major histocompatibility complex class II-matched and -mismatched lymphoblastoid cell lines to present this peptide to the T-cell clones in proliferation assays. The study reports that the epitope is restricted through HLA-DQ7 and that it can be recognized by T cells with different T-cell receptor gene rearrangements.

L112 ANSWER 40 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 13

AN 93:480335 BIOSIS

DN BA96:113935

TI VACCINATION WITH CYTOTOXIC T LYMPHOCYTE EPI-TOPE-CONTAINING PEPTIDE PROTECTS AGAINST A TUMOR INDUCED BY HUMAN PAPILLOMAVIRUS TYPE 16-TRANSFORMED CELLS.

AU FELTKAMP M C W; SMITS H L; VIERBOOM M P M; MINNAAR R P; DE JONGH B M; DRIJFHOUT J W; TER SCHEGGET J; MELIEF C J M; KAST W M

CS DEP. IMMUNOHEMATOL. BLOOD BANK, UNIV. HOSP. LEIDEN, BLDG. 1 E3-Q, P.O. BOX 9600, NL 2300 RC LEIDEN, NETHERLANDS.

SO EUR J IMMUNOL 23 (9): 1993. 2242-2249. CODEN: EJIMAF ISSN: 0014-2980

LA English

AB Cytotoxic T lymphocyte (CTL) peptide epitopes can be used for immunization of mice against lethal virus infection. To study whether this approach can be successful against virus-induced tumors we generated a B6 (H-2b) tumorigenic cell line transformed by \*\*\*human\*\*\* \*\*\*papillomavirus\*\*\* ( \*\*\*HPV\*\*\* ). This \*\*\*virus\*\*\* is detected in over 90% of all human cervical cancers. To identify vaccine candidates, we generated a set of 240 overlapping peptides derived from the \*\*\*HPV\*\*\* type 16 ( \*\*\*HPV16\*\*\* ) oncogenes E6 and E7. These peptides were tested for their ability to bind H-2Kb and H-2Db \*\*\*MHC\*\*\* class I molecules. Binding peptides were compared with the presently known peptide-binding motifs for H-2Kb and H-2Db and the predictive value of these motifs is shortly discussed. The high-affinity H2Db-binding peptide and putative CTL epitope E7 49-57 (RAHYNIIVTF) was used in vaccination studies against \*\*\*HPV\*\*\* 16-transformed tumor cells. Immunization with peptide E7 49-57 rendered mice insensitive to a subsequent challenge with \*\*\*HPV\*\*\* 16-transformed tumor cells in vivo, and induced a CTL response which lysed the tumor cells in vitro.

L112 ANSWER 41 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 14

AN 94:63982 BIOSIS

DN 97076982

TI HLA expression in pre-invasive cervical neoplasia in relation to \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* infection.

AU Glew S S; Connor M E; Snijders P J F; Stanbridge C M; Buckley C H; Walboomers J M M; Meijer C J L M; Stern P L

CS Cancer Res. Campaign, Dep. Immunology, Paterson Inst. Cancer Res., Christie Hosp. NHS Trust, Manchester M20 9BX, UK

SO European Journal of Cancer 29A (14): 1993. 1963-1970. ISSN: 0959-8049

LA English

AB A significant proportion of cervical carcinomas show loss of major histocompatibility complex human leucocyte antigen (HLA) class I expression while upregulating HLA class II expression. These changes may have direct consequences for immune surveillance of the \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) infection which is strongly associated with cervical malignancy. A relationship between changes in HLA expression and \*\*\*HPV\*\*\* infection may be evident in the evolution of premalignant disease. This immunohistological study of 104 colposcopic biopsies establishes that HLA class II expression occurs in a significant proportion of squamous epithelia showing histological evidence of wart virus infection and cervical intraepithelial neoplasia (CIN) I to III. In comparison, alteration of HLA class I expression in cervical premalignant lesions is rare. There is no correlation between the detection of high risk \*\*\*HPV\*\*\* DNA (types 16, 18, 31 and 33) by polymerase chain reaction (PCR) and the \*\*\*MHC\*\*\* class II phenotype of the lesion. This suggests that altered HLA class II expression is neither a consequence nor a prerequisite for \*\*\*HPV\*\*\* infection.

L112 ANSWER 42 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 15

AN 93:435030 BIOSIS

DN BA98:89655



TI RELATION BETWEEN SKIN CANCER HUMORAL RESPONSES TO HUMAN  
PAPILLOMAVIRUSES AND HLA CLASS II MOLECULES IN RENAL TRANSPLANT  
RECIPIENTS.

AU BAVINCK J N B; GISSMANN L; CLAAS F H J; VAN DER WOUDE F J; PERSIJN G  
G; TER SCHEGGET J; VERMEER B J; JOCHMUS I; MUELLER M; ET AL

CS DEP. DERMATOL., UNIV. HOSP. LEIDEN, RIJNSBURGERWEG 10, 2333 AA  
LEIDEN, NETH.

SO J IMMUNOL 151 (3). 1993. 1579-1586. CODEN: JOIMA3 ISSN: 0022-1767

LA English

AB Human papillomaviruses ( \*\*\*HPV\*\*\* ), especially the  
epidermodysplasia verruciformis (EV)-associated \*\*\*HPV\*\*\* 5, 8,  
14, 17, 20, and 47, are thought to play a role in the pathogenesis  
of some skin cancers in recipients of renal allografts. \*\*\*MHC\*\*\*  
class I and class II genes are involved in the cellular immune  
response to viral and tumor Ag. Little is known about humoral  
responses to \*\*\*HPV\*\*\* in recipients with and without skin  
cancer. We investigated the prevalence of antibodies to the early (E)  
protein E7 and the major capsid late (L) protein L1 of \*\*\*HPV\*\*\*  
8. In addition, we studied the association of HLA class II molecules  
with these antibody responses. The E7 and L1 open reading frames of  
\*\*\*HPV\*\*\* 8 were bacterially expressed as .beta.-galactosidase  
fusion proteins, which were purified by preparative gel  
electrophoresis. Serum samples from 36 renal transplant recipients  
with and 91 recipients without skin cancer were screened for the  
presence of IgG and IgM antibodies to \*\*\*HPV\*\*\* 8 E7 and L1, by  
Western blot analysis. The detection of anti- \*\*\*HPV\*\*\* 8 L1  
antibodies represents the immune response to \*\*\*HPV\*\*\* 8 and  
possibly other EV-associated \*\*\*HPV\*\*\*, because cross-reactivity  
between the representatives of this \*\*\*HPV\*\*\* subgenus can occur.  
The antibody responses to HLA Ag were used as controls. Recipients  
who had IgM antibodies but no IgG antibodies to L1 of \*\*\*HPV\*\*\* 8  
(patients with no apparent class switch from IgM to IgG) had skin  
cancer in 50% of cases, whereas recipients who produced IgG  
antibodies (patients with an apparently good humoral response to L1  
of \*\*\*HPV\*\*\* 8) had skin cancer in only 18% of cases. The  
estimated relative risk of skin cancer in recipients with no class  
switch, compared with the risk in those with a good humoral response,  
was 4.5 (95% confidence interval, 1.1 to 18.1). We found no  
association between the antibody response to HLA Ag and the  
occurrence of skin cancer. A strong linkage between the absent class  
switch of antibody production in response to L1 of \*\*\*HPV\*\*\* 8  
and HLA-DR7 was observed (relative risk, 26.2). Renal transplant  
recipients who have no apparent class switch from IgM to IgG  
production in response to Ag encoded by L1 of \*\*\*HPV\*\*\* 8 or  
possibly other EV-associated \*\*\*HPV\*\*\* are at an increased risk  
of skin cancer. The association with HLA-DR7 indicates a genetic  
control of skin cancer development or regression, involving genes in  
the class II region of the \*\*\*MHC\*\*\*.

L112 ANSWER 43 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1993:600875 CAPLUS

DN 119:200875

TI Comparative lymphokine secretion by cultured normal human cervical  
keratinocytes, papillomavirus-immortalized, and carcinoma cell lines

AU Woodworth, Craig D.; Simpson, Scott

CS Lab. Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA

SO Am. J. Pathol. (1993), 142(5), 1544-55

CODEN: AJPA44; ISSN: 0002-9440

DT Journal

LA English

AB The pathogenesis of cervical human papillomavirus ( \*\*\*HPV\*\*\* )  
infection is influenced by the host's immune response. This  
response depends upon secretion of specific lymphokines to recruit  
and activate immune cells at the site of infection. To examine  
whether cervical cells enhance immune-responsiveness, secretion of  
lymphokines by cultures of normal cervical cells, \*\*\*HPV\*\*\*  
-immortalized cervical lines, and carcinoma lines was compared.  
Normal cervical cells constitutively secreted interleukin-1.alpha.  
(IL-1.alpha.), IL-1.beta., IL-1 receptor antagonist, IL-6, IL-8,  
tumor necrosis factor-.alpha., and granulocyte macrophage colony  
stimulating factor. Lymphokines were also produced by exo- and  
endocervical epithelia in vivo. In contrast, 4 cervical cell lines  
immortalized by \*\*\*HPV\*\*\* DNAs and 3 carcinoma lines secreted  
selected lymphokines at significantly reduced levels.  
Interferon-gamma induced major histocompatibility class I and II  
proteins and intercellular adhesion mol.-I in normal cells, but  
results in immortal or carcinoma lines were variable. These results  
suggest that cervical epithelial cells have the potential to  
influence inflammation and immunity in the cervical mucosa.  
Furthermore, decreased expression of lymphokines and  
histocompatibility mol. by \*\*\*HPV\*\*\* -immortalized cervical



cells suggests that similar alterations might accompany persistent  
\*\*\*HPV\*\*\* infections in vivo.

L112 ANSWER 44 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 16  
AN 93:411754 BIOSIS  
DN BA96:77479

TI ANALYSIS OF \*\*\*MHC\*\*\* CLASS I AND II EXPRESSION IN RELATION TO  
PRESENCE OF \*\*\*HPV\*\*\* GENOTYPES IN PREMALIGNANT AND MALIGNANT  
CERVICAL LESIONS.

AU CROMME F V; MEIJER C J L M; SNIJDERS P J F; UYTERLINDE A; KENEMANS P;  
HELMERHORST T; STERN P L; VAN DEN BRULE A J C; WALBOOMERS J M M  
CS INST. PATHOL., SECT. MOL. PATHOL., FREE UNIV. HOSP., DE BOELELAAN  
1117, 1081 HV AMSTERDAM, NETHERLANDS.

SO BR J CANCER 67 (6). 1993. 1372-1380. CODEN: BJCAAI ISSN: 0007-0920  
LA English

AB Cervical intraepithelial neoplasia (CIN) grades I to III lesions (n =  
94) and squamous cell carcinomas of the uterine cervix (n = 27) were  
analysed for \*\*\*MHC\*\*\* classes I and II expression and presence  
of \*\*\*HPV\*\*\* genotypes. \*\*\*MHC\*\*\* class I and II expression  
was studied by immunohistochemistry and \*\*\*HPV\*\*\* typing was  
performed by general primer- and type-specific primer mediated PCR  
(GP/TS PCR). Both techniques were performed on paraffin embedded  
tissue sections. Results show disturbed \*\*\*MHC\*\*\* class I heavy  
chain expression in CIN I to CIN III, as well as in cervical  
carcinomas. Upregulated \*\*\*MHC\*\*\* class II expression on  
dysplastic epithelial cells was also found in the different CIN  
groups and carcinomas. Prevalence of \*\*\*HPV\*\*\* genotypes  
increased with the severity of the lesion, mainly due to the  
contribution of the \*\*\*HPV\*\*\* types 16 and 18. No correlation  
could be established between the presence of specific \*\*\*HPV\*\*\*  
genotypes and any \*\*\*MHC\*\*\* expression pattern in the different  
CIN groups or cervical carcinomas. In some cases these data were  
confirmed by RNA in situ hybridisation showing \*\*\*HPV\*\*\* 16 E7  
transcripts in the same dysplastic/neoplastic cells from which  
\*\*\*MHC\*\*\* status was determined. The results indicate that local  
differences may exist in the type of cellular immune response to  
\*\*\*HPV\*\*\* induced lesions.

L112 ANSWER 45 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 17  
AN 93:367983 BIOSIS  
DN BA96:53658

TI MAJOR HISTOCOMPATIBILITY COMPLEX AND HUMAN PAPILLOMAVIRUS TYPE 16 E7  
EXPRESSION IN HIGH-GRADE VULVAR LESIONS.

AU JOCHMUS I; DUERST M; REID R; ALTMANN A; BIJWARD K E; GISSMANN L;  
JENSON A B

CS DEUTSCHES KREBSFORSCHUNGSZENTRUM, FORSCHUNGSSCHWERPUNKT ANGEWANDTE  
TUMORVIROL. 2. OG WEST, IM NEUENHEIMER FELD 242, 6900 HEIDELBERG, GER.

SO HUM PATHOL 24 (5). 1993. 519-524. CODEN: HPCQA4 ISSN: 0046-8177  
LA English

AB To determine whether expression of the human papillomavirus (  
\*\*\*HPV\*\*\* ) type 16 E7 open reading frame influences expression of  
major histocompatibility complex ( \*\*\*MHC\*\*\* ) antigens on the  
surface of squamous epithelial cells, serial frozen sections from  
seven \*\*\*HPV\*\*\* type 16-positive, high-grade vulvar  
intraepithelial neoplasia (VIN 2-3) lesions were tested for viral  
transcription by RNA-RNA in situ hybridization, for \*\*\*MHC\*\*\*  
expression by immunohistochemical staining with antibodies to  
\*\*\*MHC\*\*\* class I and II molecules, and for keratinocyte  
differentiation by immunohistochemical staining with anti-filaggrin  
and cytokeratin 10 antibodies. Despite the histologic appearance of  
high-grade VIN lesions, expression patterns of cytokeratin 10 and  
filaggrin suggested a certain degree of keratinocyte differentiation  
in all specimens. These differentiation markers were especially  
prominent in parakeratotic and hyperkeratotic superficial areas,  
which did not express \*\*\*MHC\*\*\* antigens or contain E7 mRNA.  
Expression of \*\*\*MHC\*\*\* class I molecules within dysplastic  
tissues was greater than within \*\*\*HPV\*\*\* type 16-negative,  
normal vulvar epithelium from the same patients. In five of the VIN  
2-3 specimens anti- \*\*\*MHC\*\*\* class I antibodies reacted more  
strongly with cells of the basal and suprabasal layers than with  
cells of the epithelial surface. In one lesion basal cells stained  
less intensively than surface cells, whereas in another specimen all  
epithelial layers were equally \*\*\*MHC\*\*\* class I positive.  
Staining with anti- \*\*\*MHC\*\*\* class II antibodies was generally  
restricted to isolated foci, representing invading lymphocytes,  
tissue macrophages, and Langerhans cells. In two lesions, however,  
there was heterogenous keratinocyte expression of \*\*\*MHC\*\*\* class  
II proteins, perhaps due to inflammation. Major histocompatibility  
complex antigen direction was independent of the presence or  
distribution pattern of E7-specific transcripts. Hence, a correlation  
between \*\*\*MHC\*\*\* and E7 expression appears unlikely in warty VIN



lesions.

L112 ANSWER 46 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 93:538267 BIOSIS

DN BR45:125361

TI REGULATION OF \*\*\*MHC\*\*\* CLASS II AND ICAM-1 EXPRESSION BY TNF  
ALPHA AND RETINOIDS IN \*\*\*HPV\*\*\* -16 HARBORING KERATINOCYTES.

AU MAJEWSKI S; MALEJCZYK J; BREITBURD F; ORTH G; JABLONSKA S

CS DEP. DERMATOL., WARSAW SCH. MED., WARSAW, POLAND.

SO SECOND TRICONTINENTAL MEETING OF THE JSID (JAPANESE SOCIETY FOR  
INVESTIGATIVE DERMATOLOGY), SID (SOCIETY FOR INVESTIGATIVE  
DERMATOLOGY, INC.), AND ESDR (EUROPEAN SOCIETY FOR DERMATOLOGICAL  
RESEARCH), KYOTO, JAPAN, OCTOBER 28-31, 1993. J INVEST DERMATOL 101  
(3). 1993. 393. CODEN: JIDEAE ISSN: 0022-202X

DT Conference

LA English

L112 ANSWER 47 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 18

AN 93:522814 BIOSIS

DN BA96:136221

TI LACK OF ASSOCIATION OF HLA POLYMORPHISMS WITH HUMAN  
PAPILLOMAVIRUS-RELATED CERVICAL CANCER.

AU GLEW S S; DUGGAN-KEEN M; GHOSH A K; IVINSON A; SINNOTT P; DAVIDSON J;  
DYER P A; STERN P L

CS CRC DEP. IMMUNOL., PATERSON INST. FOR CANCER RES., CHRISTIE HOSP. NHS  
TRUST, MANCHESTER M20 9BX, ENGLAND, UK.

SO HUM IMMUNOL 37 (3). 1993. 157-164. CODEN: HUIMDQ ISSN: 0198-8859

LA English

AB An association of HLA-DQ3 with SCC of the cervix has been reported by  
researchers in Germany and Norway. This article documents a  
similar-sized study with patients and controls from northwest  
England. We report in detail on serologically determined HLA  
polymorphism in SCC patients with respect to \*\*\*HPV\*\*\* 16  
infection, \*\*\*MHC\*\*\* class II expression within the tumor,  
serologic response to \*\*\*HPV\*\*\*, and other relevant clinical  
variables. We have also extended our studies to include DNA-based  
analysis using PCR and SSO probes for HLA-DQ. No significant  
association of any HLA-A, -B, -C, -DR, or -DQ antigen with SCC  
patients was found. While a possible explanation of the differences  
among studies could be a reflection of disease heterogeneity, the  
several tumor and clinical factors examined do not account for the  
observed differences from previous reports. Further studies are  
needed for a greater understanding of the interaction of \*\*\*HPV\*\*\*  
and HLA type in the development of cervical neoplasia.

L112 ANSWER 48 OF 66 EMBASE COPYRIGHT 1995 ELSEVIER SCI. B.V.DUPLICATE  
19

AN 93209558 EMBASE

TI Evaluation of multiple biologic parameters in cervical carcinoma:  
High macrophage infiltration in \*\*\*HPV\*\*\* -associated tumors.

AU Connor M.E.; Davidson S.E.; Stern P.L.; Arrand J.R.; West C.M.L.

CS Experimental Radiation Oncol. Dept., Paterson Inst. for Cancer  
Research, Christie Hospital, Manchester M20 9BX, United Kingdom

SO INT. J. GYNECOL. CANCER, (1993) 3/2 (103-109).

ISSN: 1048-891X CODEN: IJGCEN

CY United States

DT Journal

FS 004 Microbiology

005 General Pathology and Pathological Anatomy

010 Obstetrics and Gynecology

016 Cancer

LA English

SL English

AB A number of diverse biologic parameters have been assessed prior to  
treatment in a series of patients with cervical carcinoma. Factors  
analyzed were \*\*\*HPV\*\*\* DNA presence, \*\*\*MHC\*\*\* class I  
expression, expression of the oncofetal antigen 5T4, the proportions  
of macrophages, lymphocytes and granulocytes in cell suspensions  
prepared from tumors, in vitro colony-forming efficiency (CFE) and a  
measure of intrinsic radiosensitivity, surviving fraction at 2 Gy.  
Several associations were found. First, \*\*\*HPV\*\*\* DNA-negative  
tumors contained a small, but significant, decreased number of tumor  
infiltrating macrophages compared with \*\*\*HPV\*\*\* DNA-positive  
tumors. Secondly, patients with \*\*\*HPV\*\*\* -positive tumors were  
significantly younger than those where no \*\*\*HPV\*\*\* was  
detected. Thirdly, loss of one or more specific alleles in  
\*\*\*MHC\*\*\* class I positive tumors resulted in higher numbers of  
tumor lymphocytes and CFEs. Finally, strong expression of the 5T4  
antigen was related to a reduction in the proportion of macrophages  
in tumor cell suspensions. In addition, for stage I and II patients  
expression of the \*\*\*MHC\*\*\* class I molecule was associated with



improved survival compared with patients with tumors where loss of expression was seen.

L112 ANSWER 49 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1993:227420 CAPLUS

DN 118:227420

TI Human YB-1 protein binding to enhancer of \*\*\*human\*\*\*  
\*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 18

AU Spitkovsky, D. D.; Royer, H. D.; Mazurenko, N. N.; Mikhaleva, I. I.;  
Prudchenko, I. A.; Korbukh, I. A.; Sukhova, N. M.; Kisseijov, F. L.

CS Can. Res. Cent., Inst. Carcinogen., Moscow, 115478, Russia

SO Mol. Biol. (Moscow) (1993), 27(1), 81-91

CODEN: MOBIBO; ISSN: 0026-8984

DT Journal

LA Russian

AB Enhancer sequences of \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
\*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 18 were used for screening of a  
HeLa cell cDNA library in .lambda. gt11 using the protein binding  
method. Clones with YB-1 gene homol. sequences were isolated. The  
gene codes for a protein which binds the regulatory region of gene Y  
for major histocompatibility complex class II (HLA 11). The YB-1  
transcripts were found in all samples of cervical carcinomas. To  
analyze the protein, rabbit antibodies were produced to a synthetic  
peptide, which corresponds to the most hydrophilic region of the  
protein. This antipeptide serum permitted identification of a  
nuclear 42K protein in HeLa cells as well as in normal fibroblasts.

L112 ANSWER 50 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS

AN 93:331202 BIOSIS

DN BR45:25927

TI ANALYSIS OF \*\*\*MHC\*\*\* CLASS I AND II EXPRESSION IN RELATION TO  
PRESENCE OF \*\*\*HPV\*\*\* GENOTYPES IN PREMALIGNANT AND MALIGNANT  
CERVICAL LESIONS

AU STUKART M J; CROMME F V; MEIJER C J L M; SNIJDERS P J F; UYTERLINDE  
A; KENEMANS P; WALBOOMERS J M M

CS INST. PATHOL., SECT. MOLECULAR PATHOL., FREE UNIV. HOSP., DE  
BOELELAAN 1117, 1081 HV AMSTERDAM, NETHERLANDS.

SO KEYSTONE SYMPOSIUM ON MOLECULAR IMMUNOLOGY OF VIRUS INFECTIONS, TAOS,  
NEW MEXICO, USA, MARCH 17-24, 1993. J CELL BIOCHEM SUPPL 0 (17 PART  
D). 1993. 70. CODEN: JCBSD7

DT Conference

LA English

L112 ANSWER 51 OF 66 SCISEARCH COPYRIGHT 1995 ISI (R)

AN 93:219886 SCISEARCH

GA The Genuine Article (R) Number: KV880

TI ANALYSIS OF \*\*\*MHC\*\*\* CLASS-I AND CLASS-II EXPRESSION IN  
RELATION TO PRESENCE OF \*\*\*HPV\*\*\* GENOTYPES IN PREMALIGNANT AND  
MALIGNANT CERVICAL LESIONS

AU STUKART M J (Reprint); CROMME F V; MEIJER C J L M; SNIJDERS P J F;  
UYTERLINDE A; KENEMANS P; WALBOOMERS J M M

CS FREE UNIV AMSTERDAM HOSP, INST PATHOL, 1081 HV AMSTERDAM,  
NETHERLANDS; FREE UNIV AMSTERDAM HOSP, DEPT GYNAECOL, MOLEC PATHOL  
SECT, 1081 HV AMSTERDAM, NETHERLANDS

CYA NETHERLANDS

SO JOURNAL OF CELLULAR BIOCHEMISTRY, (13 MAR 1993) Supp. 17D, pp. 70.  
ISSN: 0730-2312.

DT Conference; Journal

FS LIFE

LA ENGLISH

REC No References

L112 ANSWER 52 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 20

AN 93:253958 BIOSIS

DN BA95:133133

TI HLA CLASS I EXPRESSION AND \*\*\*HPV\*\*\* -16 SEQUENCES IN PREMALIGNANT  
AND MALIGNANT LESIONS OF THE CERVIX

AU TORRES L M; CABRERA T; CONCHA A; OLIVA M R; RUIZ-CABELLO F; GARRIDO F

CS SERV. DE ANALISIS CLINICOS E IMMUNOL., HOSP. VIRGEN DE LAS NIEVES,  
AVD. CORONEL MUNOZ N 2, 18014 GRANADA, SPAIN.

SO TISSUE ANTIGENS 41 (2). 1993. 65-71. CODEN: TSANA2 ISSN: 0001-2815

LA English

AB A series of 10 normal cervix epithelia, 38 condylomas, 17 CIN  
(cervical intraepithelial neoplasia) I/II (low-grade CIN), 10 CIN III  
(high-grade CIN), 27 squamous cell carcinomas and 7 adenocarcinomas  
of the cervix were studied in paraffin-embedded sections for the  
expression of \*\*\*MHC\*\*\* class I antigens, using antibodies  
against HLA antigens and the immunoperoxidase techniques. A PCR  
technique was also used to evaluate the presence of \*\*\*HPV\*\*\* -16  
DNA. All samples from normal tissue, benign, premalignant and CIN  
III lesions expressed HLA class I antigens. However, 15% of the



invasive carcinomas completely lacked HLA-B and HLA-C antigen expression, 20% presented a heterogenous pattern and 2 cases lacked HLA-B and HLA-C heavy chain but retained .beta.2-microglobulin. \*\*\*MHC\*\*\* class I antigen expression on tumors was compared with clinical-pathological parameters. The absence of expression of HLA class I molecules was significantly associated with the Glanz histoprognotic index of malignancy. \*\*\*HPV\*\*\* -16 sequences were detected in 60% of the condylomas, 88% of the CIN I/II, 80% of the CIN III and 82% of the cervical carcinomas. Eight-six per cent of the tumors expressing HLA class I antigen presented \*\*\*HPV\*\*\* -16, whereas only 40% of the nonexpressing tumors did. Our results lead us to the following conclusions: a) HLA class I losses occurred when the tumor became invasive, and in tumors of a more aggressive histological type; b) The presence of \*\*\*HPV\*\*\* -16 was associated with tumors expressing HLA class I antigens.

L112 ANSWER 53 OF 66 COPYRIGHT 1995 INFO. ACCESS CO.

AN 92:203772 NLDB  
 TI MEDICAL GRANT MONITOR: A REGULAR UPDATE ON ALL MAJOR RESEARCH AWARD GRANTS--Allergy and Infectious Diseases  
 SO Medical Research Funding News, (13 May 1992) .  
 ISSN: 1052-9152.  
 PB Faulkner & Gray, Inc.  
 DT Newsletter  
 LA English  
 WC 470

L112 ANSWER 54 OF 66 CAPLUS COPYRIGHT 1995 ACS

AN 1992:590111 CAPLUS  
 DN 117:190111  
 TI \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* peptides and organisms producing said peptides for use in vaccine compositions  
 IN Thomas, Elaine Kinney; Chen, Lieping; Blake, James; Hellstrom, Karl Erik; Hellstrom, Ingegerd; Hu, Shiu Lok  
 PA Bristol-Myers Squibb Co., USA  
 SO PCT Int. Appl., 82 pp.  
 CODEN: PIXXD2  
 PI WO 9205248 A1 920402  
 DS W: AU, CA, JP, KR, NO  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE  
 AI WO 91-US7081 910926  
 PRAI US 90-588384 900926  
 DT Patent  
 LA English  
 AB Immunogenic peptides corresponding to peptides expressed in mammalian cells in response to \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) infection are described. Recombinant organisms (such as vaccinia virus or tumor cells) producing such a peptide, or the peptide, can be used to treat \*\*\*HPV\*\*\* infections. Recombinant vaccinia virus expressing either the \*\*\*HPV\*\*\* E7 or E6 gene, and mammalian cell expression plasmids contg. these genes, were prepd. Mice were injected i.p. with \*\*\*HPV\*\*\* E7 epitope-producing fibroblasts, then challenged by s.c. administration of a tumorigenic dose of M2 melanoma cells transfected with \*\*\*HPV16\*\*\* E7 expression vector. A transient development of tumors followed by tumor regression was obsd.

L112 ANSWER 55 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 21

AN 92:501950 BIOSIS  
 DN BA94:120475  
 TI INDUCTION OF CYTOTOXIC T LYMPHOCYTES WITH PEPTIDES IN-VITRO IDENTIFICATION OF CANDIDATE T-CELL EPITOPES IN \*\*\*HUMAN\*\*\* \*\*\*PAPILLOMA\*\*\* \*\*\*VIRUS\*\*\* .  
 AU STAUSS H J; DAVIES H; SADOVNIKOVA E; CHAIN B; HOROWITZ N; SINCLAIR C  
 CS IMP. CANCER RES. FUND, HUM. TUM. IMMUNOL. GROUP, UNIVERSITY COLL., MIDDLESEX HOSP., LONDON W1P 8BT, UK.  
 SO PROC NATL ACAD SCI U S A 89 (17). 1992. 7871-7875. CODEN: PNASA6  
 ISSN: 0027-8424  
 LA English  
 AB A set of overlapping peptides corresponding to the L1, E6, and E7 proteins of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* 16 was tested for their ability to bind to \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\* \*\*\*I\*\*\* \*\*\*molecules\*\*\* and to stimulate cytotoxic T-lymphocyte (CTL) responses in vitro. A class I binding assay using intact RMA-S cells showed that 20 of the 99 \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* peptides bound to H-2Kb and/or Db molecules. Fifteen of the 20 class I-binding peptides stimulated primary CTL responses, whereas peptides that were negative in the binding assay failed to do so. Peptide-induced CTLs recognized the immunizing peptide very



efficiently, requiring no more than 1-10 nM peptide for target cell lysis. However, two observations were made that have important implications for the design of peptide-based vaccines for inducing CTLs. (i) Not all major histocompatibility complex-binding peptides that contained known motifs characteristic of naturally processed peptides induced CTLs. (ii) The efficiency of CTL lysis was strongly decreased when the size of the target peptide differed by only one amino acid residue from that of the immunizing peptide. We conclude that peptides chosen for vaccination must correspond in length to naturally processed peptides.

L112 ANSWER 56 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 22

AN 92:456852 BIOSIS

DN BA94:98252

TI HLA CLASS II ANTIGEN EXPRESSION IN HUMAN PAPILLOMAVIRUS-ASSOCIATED CERVICAL CANCER.

AU GLEW S S; DUGGAN-KEEN M; CABRERA T; STERN P L

CS CANCER RES. CAMPAIGN DEP. IMMUNOL., PATERSON INST. CANCER RES., CHRISTIE HOSP., MANCHESTER M20 9BX, UK.

SO CANCER RES 52 (14). 1992. 4009-4016. CODEN: CNREA8 ISSN: 0008-5472

LA English

AB The observation that tumor cells of some neoplasms display major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II molecules may be of functional significance, influencing the progression of malignancy by allowing the cancer cells to present antigen to the immune system. In the normal cervix, class II molecules are expressed by columnar but not squamous epithelium. The pattern of \*\*\*MHC\*\*\* class II expression in cervical carcinomas has been documented using immunohistochemical methods. Of 53 cervical squamous carcinomas examined for \*\*\*MHC\*\*\* class II expression, only 17% maintained a negative phenotype characteristic of the epithelium from which they were derived, while the remaining tumors exhibited either uniform (45%) or heterogeneous (38%) expression. Tumor areas which were class II positive also express class II associated invariant chain and the adhesion molecules lymphocyte function antigen 3 and intercellular adhesion molecule 1. The DR, DP, and DQ class II \*\*\*MHC\*\*\* subloci are differentially expressed, suggesting independent regulation. There is a trend for tumors with the uniform class II phenotype to predominantly express DR antigen, whereas tumors of the heterogeneous class II phenotype express with equal frequency either DR or DP antigens dominantly. There is no apparent influence of class II status on lymphocyte infiltration of the tumors. The presence of human papillomavirus 16 DNA in the cervical carcinoma specimens was analyzed by Southern blotting of restriction enzyme digested DNA and no correlation between the presence of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* and \*\*\*MHC\*\*\* class II expression was found.

L112 ANSWER 57 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 23

AN 92:305904 BIOSIS

DN BA94:19054

TI INDUCTION OF CYTOTOXIC T LYMPHOCYTES SPECIFIC FOR A SYNGENEIC TUMOR EXPRESSING THE E6 ONCOPROTEIN OF HUMAN PAPILLOMAVIRUS TYPE 16.

AU CHEN L; MIZUNO M T; SINGHAL M C; HU S-L; GALLOWAY D A; HELLSTROM I; HELLSTROM K E

CS BRISTOL-MYERS SQUIBB PHARMACEUTICAL RES. INST., 3005 FIRST AVE., SEATTLE, WASH. 98121.

SO J IMMUNOL 148 (8). 1992. 2617-2621. CODEN: JOIMA3 ISSN: 0022-1767

LA English

AB Human papillomavirus ( \*\*\*HPV\*\*\* ) type 16 has been implicated in the etiology of cervical carcinomas, but it is unknown whether \*\*\*HPV\*\*\* -specific immunity can function in controlling the growth of \*\*\*HPV\*\*\* -associated carcinomas. We previously demonstrated that CD8+ T lymphocytes can inhibit the in vivo outgrowth of murine tumors cells transfected with the \*\*\*HPV\*\*\* -16 E7 gene have now established a murine model to study the CTL responses to the E6 oncoprotein of \*\*\*HPV\*\*\* -16. Immunization of C3H/HeN mice with syngeneic fibroblasts expressing a transfected \*\*\*HPV\*\*\* -16 E6 gene induced regression of transplanted tumors expressing this gene. Populations of CTL isolated from the spleens of mice whose E6+ tumors had regressed were shown to specifically lyse E6+ target cells. The cytolytic activity was mediated by CD8+ CTL in a \*\*\*MHC\*\*\* -restricted pattern. These data and our previous findings with transfected tumor cells expressing the E7 gene, support the conclusion that tumor cells associated with \*\*\*HPV\*\*\* -16 can be inhibited by CTL specific for molecules encoded by the \*\*\*HPV\*\*\* -16 and E6 and E7 genes.

L112 ANSWER 58 OF 66 CANCERLIT DUPLICATE 24

AN 92097117 CANCERLIT

TI LEUKOREGULIN AND GAMMA-INTERFERON INHIBIT HUMAN PAPILLOMAVIRUS TYPE



16 GENE TRANSCRIPTION IN HUMAN PAPILLOMAVIRUS-IMMORTALIZED HUMAN  
CERVICAL CELLS.

AU Woodworth C D; Licht U; Simpson S; Evans C H; DiPaolo J A  
CS Laboratory of Biology, National Cancer Institute, Bethesda, Maryland  
20892.

SO Cancer Res, (1992). Vol. 52, No. 2, pp. 456-63.

Journal code: CNF. ISSN: 0008-5472.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals

LA English

OS MEDLINE 92097117

EM 9203

AB The human papillomavirus ( \*\*\*HPV\*\*\* ) transforming genes E6 and E7 are retained and expressed in the majority of cervical cancers implying an important role for these proteins in maintenance of the malignant phenotype. Leukoregulin (LR) and recombinant gamma-interferon (r-IFN-gamma), lymphokines secreted by immune cells present in regressing \*\*\*HPV\*\*\* infections, inhibited transcription of E6/E7 RNAs in several human cervical epithelial cell lines immortalized by recombinant \*\*\*HPV\*\*\* -16, -18, and -33 DNAs. r-IFN alpha was not effective. Reduction in E6/E7 RNA expression was accompanied by inhibition of cell proliferation coincident with an increase in epidermal transglutaminase activity, a marker of squamous differentiation. LR and r-IFN gamma enhanced transcription of class 1 cell surface histocompatibility antigens (HLA) and r-IFN gamma additionally induced HLA class 2 expression. \*\*\*HPV\*\*\* -immortalized cells developed partial resistance to the growth inhibitory effects of lymphokines after malignant transformation or extended propagation in culture. This is the first demonstration that LR and r-IFN gamma selectively inhibit transcription of \*\*\*HPV\*\*\* -transforming genes and suggests a molecular mechanism by which these lymphokines participate in regression of premalignant cells.

L112 ANSWER 59 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 25

AN 92:282442 BIOSIS

DN BA94:7092

TI DEFINITION OF IMMUNOGENIC DETERMINANTS OF THE HUMAN PAPILLOMAVIRUS  
TYPE 16 NUCLEOPROTEIN E7.

AU ALTMANN A; JOCHMUS-KUDIELKA I; FRANK R; GAUSEPOHL H; MOEBIUS U;  
GISSMANN L; MEUER S C

CS DEP. APPLIED IMMUNOLOGY, INSTITUTE RADIOLOGY PATHOPHYSIOLOGY, IM  
NEUENHEIMER FELD 280, D-6900 HEIDELBERG, GER.

SO EUR J CANCER 28 (2-3). 1992. 326-333. CODEN: EJCAEL ISSN: 0959-8049

LA English

AB Specific T lymphocyte lines and T cell clones were established from peripheral blood mononuclear cells of asymptomatic seropositive individuals employing synthetic peptides which correspond to the sequence of the human papillomavirus ( \*\*\*HPV\*\*\* ) type 16 transforming protein E7. Specificity analysis of T cells as determined by means of [3H] thymidine incorporation after stimulation with individual peptides revealed three immunogenic determinants of E7 that are recognised in association with at least two different HLA haplotypes. One N-terminal region (aminoacids 5-18) was recognised by one T cell line. T cell clones and the corresponding T cell line established from another donor responded to different N-terminal (17-38) and to a C-terminal region (69-86). The N-terminal sequence 5-18 and the C-terminal determinant contain a periodicity of hydrophilic and hydrophobic residues that have been found in many T cell epitopes. Phenotypic characterisation of T cell clones by indirect immunofluorescence revealed that the T cell clones expressed the CD4 surface glycoprotein suggesting that the specific E7 determinants were recognised in association with major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II molecules. With regard to functional properties, at least three T cell clones exhibited specific cytotoxic activity towards autologous B lymphocytes transformed by Epstein-Barr virus in the presence of the relevant \*\*\*HPV16\*\*\* E7 peptides. The implications of these results regarding the development of vaccination strategies and host-virus interaction are discussed.

L112 ANSWER 60 OF 66 CANCERLIT DUPLICATE 26

AN 92094170 CANCERLIT

TI T-CELL IMMUNOTHERAPY OF CANCER.

AU Melief C J; Kast W M

CS Division of Immunology, The Netherlands Cancer Institute, Amsterdam.

SO Res Immunol, (1991). Vol. 142, No. 5-6, pp. 425-9.

Journal code: R6E. ISSN: 0923-2494.

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)



FS MEDL; L; Priority Journals  
LA English  
OS MEDLINE 92094170  
EM 9203

AB In animal systems, complete and permanent eradication of tumours can be achieved by adoptive transfer of \*\*\*MHC\*\*\* -restricted T cells, combined with IL2. In certain types of human cancer (melanoma and perhaps renal cell carcinoma), tumour-specific T cells are probably the therapeutically most active cells among LAK or TIL cells. To prove these points, it is necessary to conduct trials with cloned tumour-specific T cells. Other potentially immunogenic tumors are cervical carcinoma, associated with \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\*, and Burkitt's lymphoma, associated with Epstein-Barr virus. Most other human tumours, caused by subtle mutations in proto-oncogenes, are likely to be poorly or non-immunogenic. It is worthwhile trying to overcome this by vaccination with IL2 or IFN gamma-producing tumour cells or by deliberate vaccination with desirable targets for tumour-specific CTL such as the products of point-mutated oncogenes, including ras (Jung and Schleusener, 1991) and p53 (Rodríguez et al., 1990; Halevy et al., 1990), provided the relevant peptides are processed and bound to \*\*\*MHC\*\*\* class I molecules. Other potential targets are breakpoint peptides of translocated oncogene products such as bcr/abl (Van Denderen et al., 1990). In viral systems, it has already been established that peptide vaccination for protective CTL induction is feasible (Aichele et al., 1989; Schulz et al., 1991; Kast et al., 1991). (46 Refs)

L112 ANSWER 61 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS  
AN 91:526679 BIOSIS  
DN BA92:138139  
TI KILLER CELL LINES AGAINST SHOPE CARCINOMA CELLS IN RABBITS.  
AU TAKAHASHI M; YAMADE I; SETO A  
CS DEP. MICROBIOL., SHIGA UNIV. MED. SCI., SETA, OTSU 520-21, JPN.  
SO CANCER LETT 59 (3). 1991. 243-250. CODEN: CALEDQ ISSN: 0304-3835  
LA English

AB Killer cell activity against Shope carcinoma cells was not detected in PBL nor in spleen cells from tumor-bearing B/J rabbits, but was induced by in vitro culture of these cells in the presence of IL-2 and X-irradiated carcinoma cells. HTLV-I-transformed killer cell lines were successfully obtained by the culturing of PBL from an HTKV-I-infected and tumor-bearing Chbb:HM rabbit. These killer cells included large cells with azurophilic granules in the cytoplasm and with a reniform nucleus, thus resembling large granular lymphocytes. The killer activity was similar against the Vx2K cell line from a random-bred rabbit and SBC cell lines from B/J rabbit, suggesting the absence of \*\*\*MHC\*\*\* restriction.

L112 ANSWER 62 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 27  
AN 91:181239 BIOSIS  
DN BA91:95988  
TI THE INDUCTION OF CYTOTOXIC T-LYMPHOCYTE PRECURSOR CELLS BY RECOMBINANT VACCINIA \*\*\*VIRUS\*\*\* EXPRESSION \*\*\*HUMAN\*\*\* \*\*\*PAPILLOMAVIRUS\*\*\* TYPE 16 L1.  
AU ZHOU J; MCINDOE A; DAVIES H; SUN X-Y; CRAWFORD L  
CS ICRF TUMOUR VIRUS GROUP, DEP. PATHOL., UNIV. CAMBRIDGE, TENNIS COURT ROAD, CAMBRIDGE CB2 1QP, UK.  
SO VIROLOGY 181 (1). 1991. 203-210. CODEN: VIRLAX ISSN: 0042-6822  
LA English

AB Expression of the major coat protein L1 of \*\*\*human\*\*\* \*\*\*papillomavirus\*\*\* type 16 by recombinant vaccinia \*\*\*viruses\*\*\* using a vaccinia late promoter and their use in generating antibodies have already been reported (Zhou et al., 1990). We have now constructed recombinant vaccinia viruses (VVs) which express the L1 protein from an early promoter with the intention of inducing cell-mediated immunity. This necessitated the removal of sequence motifs (TTTTNT) from the L1 gene which would otherwise have caused transcription termination when expressed from a vaccinia virus early promoter. The nucleotide sequence was mutated to retain the correct amino acid sequence of the L1 protein. Full-length mRNA and L1 protein were generated in cells infected with the recombinant virus containing the mutant sequence, whereas the wild-type sequence generated only truncated mRNA and no detectable protein. Mice were immunized with VV expressing L1 from the mutant sequence and from the wild-type sequence in constructs with either early or late vaccinia virus promoters. Only the early promoter construct were effective in priming cytotoxic T lymphocytes (CTL). Moreover the mutant sequence was significantly more effective than the wild-type sequence. The same L1 sequences, expressed from a vaccinia virus late promoter or coexpressed with \*\*\*MHC\*\*\* Class I molecules also expressed from a late promoter, produced high levels of L1 protein in both cases but



nevertheless failed to elicit CTL activity. This is the first report of an \*\*\*HPV\*\*\* -specific CTL response and we have reaffirmed the importance of choosing the correct promoter and sequence expressed when using recombinant vaccinia viruses to induce cytotoxic T lymphocytes. These data are relevant for the design of vaccines to generate cell-mediated immunity against human papillomavirus infection.

L112 ANSWER 63 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 28  
AN 91:49209 BIOSIS  
DN BA91:27490  
TI DEFINITION OF MURINE T HELPER CELL DETERMINANTS IN THE MAJOR CAPSID PROTEIN OF HUMAN PAPILLOMAVIRUS TYPE 16.  
AU DAVIES D H; HILL C M; ROTHBARD J B; CHAIN B M  
CS IMPERIAL CANCER RES. FUND TUMOUR IMMUNOL. UNIT, DEP. BIOL., MEDAWAR BUILD., UNIV. COLL. LONDON, GOWER ST., LONDON WC1E 6BT.  
SO J GEN VIROL 71 (11). 1990. 2691-2698. CODEN: JGVIAI ISSN: 0022-1317  
LA English  
AB Three murine major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II-restricted T cell determinants were identified in the major capsid protein L1 of human papillomavirus ( \*\*\*HPV\*\*\* ) type 16. Peptides derived from \*\*\*HPV\*\*\* -16 L1, which contain putative T cell epitopes located by a predictive algorithm, were synthesized and tested for lymphoproliferative activity by direct immunization, followed by in vitro assay of responses to peptides or recombinant \*\*\*HPV\*\*\* -16 L1. The \*\*\*MHC\*\*\* restriction of the stimulatory peptides was determined using blocking monoclonal antibodies against class II molecules. The responses, which were specific for the priming peptides alone, cross-reacted with recombinant L1 but not with analogous peptides derived from other \*\*\*HPV\*\*\* types.

L112 ANSWER 64 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 29  
AN 91:93348 BIOSIS  
DN BA91:52238  
TI LOSS OF \*\*\*MHC\*\*\* CLASS-I EXPRESSION IN CERVICAL CARCINOMAS.  
AU CONNOR M E; STERN P L  
CS DEP. IMMUNOL., PATERSON INST. CANCER RES., CHRISTIE HOSPITAL HOLT RADIUM INST., MANCHESTER M20 9BX, UK.  
SO INT J CANCER 46 (6). 1990. 1029-1034. CODEN: IJCNAA ISSN: 0020-7136  
LA English  
AB The expression of \*\*\*MHC\*\*\* class-I antigens was analyzed in 67 cervical carcinoma biopsies; 16% of the biopsies showed complete or heterogeneous loss of HLA expression as judged by reactivity with antibodies recognizing monomorphic determinants of the class-I heavy chain bound to .beta.2 microglobulin (.beta.2m). In addition, other biopsies showed a loss in expression of particular allelic products: 23% for HLA-A2; 17% for HLA-A3; 23% for HLA-Bw4 and 19% for HLA-Bw6. Three biopsies showed changes at 2 alleles, 2 of which were at both HLA-A and -B loci. Down-regulation of class-I expression may be virally mediated and \*\*\*HPV\*\*\* DNA is frequently found in cervical carcinomas. However, there appeared to be no direct correlation between the detection \*\*\*HPV\*\*\* 16 or 18 DNA in these tumours and changes in HLA expression. There was also no correlation with the expression of the oncofoetal antigen 5T4. Our results show that a significant proportion (at least 30%) of the cervical carcinomas showed some alteration in \*\*\*MHC\*\*\* class-I expression. Such changes may allow tumours to evade immune surveillance with more rapid progression. There was, however, no correlation with tumour type, degree of differentiation or stage of disease at presentation.

L112 ANSWER 65 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 30  
AN 88:245629 BIOSIS  
DN BA85:124031  
TI EXPRESSION OF MAJOR HISTOCOMPATIBILITY CLASS II ANTIGENS BY LANGERHANS' CELLS IN CERVICAL INTRAEPITHELIAL NEOPLASIA.  
AU HUGHES R G; NORVAL M; HOWE S E M  
CS SIMPSON MEML. MATERNITY PAVILION, LAURISTON PLACE, EDINBURGH EH3 9YW, SCOTLAND.  
SO J CLIN PATHOL (LOND) 41 (3). 1988. 253-259. CODEN: JCPAAK ISSN: 0021-9746  
LA English  
AB Cervical biopsy samples from 67 patients who had various grades of cervical intraepithelial neoplasia (CIN) or who showed evidence, in the form of koilocytosis, of human papillomavirus ( \*\*\*HPV\*\*\* ) infection of the uterine cervix, and from 10 women with normal cervixes were examined. Cryostat sections from the biopsy samples were stained using monoclonal antibodies to T6, a Langerhans' cell marker, and to major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II antigens (HLA-DP, DQ, and DR). Epithelial Langerhans' cells were reduced in number and showed changed morphology and distribution in



kilocytic lesions and in all grades of CIN ( $p < 0.01$ ) except CIN I. HLA-DR expression by Langerhans' cells was significantly increased in kilocytic lesions and in CIN grades I and II ( $p < 0.05$ ); HLA-DQ expression was significantly increased in all grades of CIN ( $p < 0.05$ ) with the increase being most pronounced in CIN I ( $p < 0.01$ ). Columnar epithelium expressed \*\*\*MHC\*\*\* class II antigens in all samples tested and squamous epithelium in four of 29 cases of CIN III. These findings support the view that there is a localised disturbance of immune function in both neoplastic cervical epithelium and that infected with papillomavirus.

L112 ANSWER 66 OF 66 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 31

AN 88:439801 BIOSIS

DN BA86:91899

TI EPIDERMAL LANGERHANS CELLS DERMAL DENDRITIC CELLS AND KERATINOCYTES IN VIRAL LESIONS OF SKIN AND MUCOUS MEMBRANES AN IMMUNOHISTOCHEMICAL STUDY.

AU DRIJKONINGEN M; DE WOLF-PEETERS C; DEGREEF H; DESMET V  
CS UNIV. ZIEKENHUIS SINT RAFAEL, LAB. VOOR HISTO- EN CYTOCHEMIE, MINDERBROEDERSSTRAAT12, B-3000 LEUVEN, BELGIUM.

SO ARCH DERMATOL RES 280 (4). 1988. 220-227. CODEN: ADREDL ISSN: 0340-3696

LA English

AB We wanted to evaluate the eventual expression of viral antigens and \*\*\*MHC\*\*\* class II products by keratinocytes as well as the alterations of epidermal Langerhans cells and dermal dendritic cells in viral lesions of skin and mucous membranes. Therefore we investigated 68 biopsy specimens of protracted viral lesions, such as warts, condylomas, and mollusca contagiosa, and of rapidly resolving viral lesions such as herpes simplex virus infection. For this we used immunohistochemical staining techniques and several monoclonal and polyclonal antisera. In most cases investigated viral antigens ( \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* antigens or herpes simplex \*\*\*virus\*\*\* type 1 antigens) could be demonstrated in keratinocytic nuclei. Except for a few viral lesions in which epidermal Langerhans cells were rather numerous, epidermal Langerhans cells were reduced in number or absent in almost all viral lesions. Moreover, epidermal Langerhans cells and dermal dendritic cells showed changes in morphology, distribution, and immunophenotype. These alterations may be caused by a toxic effect of the virus on dendritic cells. HLA-DR+ keratinocytes could be identified in few viral lesions only; HLA-DQ+ keratinocytes were seen. Possible explanations for this lack of \*\*\*MHC\*\*\* class II expression by keratinocytes are discussed.

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L150 20 DUP REM L149 (22 DUPLICATES REMOVED)

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L150 ANSWER 1 OF 20 CAPLUS COPYRIGHT 1995 ACS

AN 1995:442210 CAPLUS

DN 122:211608

TI Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein

AU Wucherpfennig, Kai W.; Strominger, Jack L.

CS Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA

SO Cell (Cambridge, Mass.) (1995), 80(5), 695-705

CODEN: CELLB5; ISSN: 0092-8674

DT Journal

LA English

AB Structural similarity between viral T cell epitopes and self-peptides could lead to the induction of an autoaggressive T cell response. Based on the structural requirements for both \*\*\*MHC\*\*\* class II binding and TCR recognition of an immunodominant myelin basic protein (MBP) peptide, criteria for a data search were developed in which the degeneracy of \*\*\*amino\*\*\* \*\*\*acid\*\*\* side chains required for \*\*\*MHC\*\*\* class II binding



and the conservation of those required for T cell activation were considered. A panel of 129 peptides that matched the mol. mimicry motif was tested on seven MBP-specific T cell clones from multiple sclerosis patients. Seven viral and one bacterial peptide efficiently activated three of these clones. Only one peptide could have been identified as a mol. mimic by sequence alignment. The observation that a single T cell receptor can recognize quite distinct but structurally related peptides from multiple pathogens has important implications for understanding the pathogenesis of autoimmunity.

L150 ANSWER 2 OF 20 COPYRIGHT 1995 PJB

AN 94:17778 PHIN  
DN S00420996  
DED 22 Nov 1994  
TI British Technology Group (BTG) seeks new development capital  
SO Scrip (1994) No. 1977 p16  
DT Newsletter  
FS FULL

L150 ANSWER 3 OF 20 CAPLUS COPYRIGHT 1995 ACS

AN 1994:455887 CAPLUS  
DN 121:55887  
TI Antigenic peptides binding class I \*\*\*MHC\*\*\* proteins and their diagnostic and therapeutic uses  
IN Kubo, Ralph T.; Grey, Howard M.; Sette, Alessandro; Celis, Esteban  
PA Cytel Corp., USA  
SO PCT Int. Appl., 149 pp.  
CODEN: PIXXD2  
PI WO 9403205 A1 940217  
DS W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN  
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
AI WO 93-US7421 930806  
PRAI US 92-926666 920807  
US 93-27746 930305  
DT Patent  
LA English  
AB Antigenic peptides capable of specifically binding selected \*\*\*MHC\*\*\* antigens and inducing T cell activation in T cells restricted by the corresponding \*\*\*MHC\*\*\* allele are described. The peptides are used to elicit an immune response against a desired antigen. HLA-A antigens were purified by affinity chromatog. against allele-specific or monoclonal antibodies. Peptides remaining bound to the HLA-A antigens after affinity purifn. were eluted at acidic pH, fractionated by HPLC and individual fractions immobilized and sequenced. Residues essential for binding to the antigen were detected during sequencing were obsd. in complex fractions by being the major \*\*\*amino\*\*\* \*\*\*acid\*\*\* in a given cycle of the sequencing reaction. A decapeptide specific for an HLA-A3.2 antigen was obsd. with position 2 V, L; or M, position 3 Y or D; position 7 I; position 8 Q or N; and positions 9 and 10 both K. Similarly, motifs were obsd. for HLA-A1, A11, and A24.1. Antigens contg. these motifs were searched for in sequence databases and a no. of such sequences were found in tumor-specific antigens and viral proteins. These peptides were used as probes for the assay of the cognate HLA-A antigens.

L150 ANSWER 4 OF 20 CAPLUS COPYRIGHT 1995 ACS

AN 1995:8346 CAPLUS  
DN 122:7346  
TI Role of HLA-A motifs in identification of potential CTL epitopes in human papillomavirus type 16 E6 and E7 proteins  
AU Kast, W. Martin; Brandt, Remco M. P.; Sidney, John; Drijfhout, Jan Wouter; Kubo, Ralph T.; Grey, Howard M.; Melief, Cornelis J. M.; Sette, Alessandro  
CS Dep. Immunohematol., Univ. Hosp., Leiden, Neth.  
SO J. Immunol. (1994), 152(8), 3904-12  
CODEN: JOIMA3; ISSN: 0022-1767  
DT Journal  
LA English  
AB The authors have measured the binding affinity for five HLA-A alleles: HLA-A1 (A\*0101), A2.1 (A\*0201), A3 (A\*0301), A11 (A\*1101), and A24 (A\*2401); of a set of all possible nonamer peptides of human papillomavirus type 16 E6 and E7 proteins. High affinity binding peptides were identified for each of the alleles, thus allowing the authors to select several candidates for CTL-based vaccines. Moreover, this unbiased set of peptides allowed an evaln. of the



predictive value of HLA motifs derived either from the anal. of sequencing of pools of naturally processed peptides or from the binding anal. of polyaniline nonameric peptides that differed in the \*\*\*amino\*\*\* \*\*acids\*\*\* (aa) present at the anchor positions. Whereas pool sequence-derived motifs were present in only 27% of high affinity binders, the more expanded motif, based on anal. of different aa substitutions at the anchor positions, was present in 73% of high affinity binders. Furthermore, it was found that the presence of anchor residues in a peptide was in itself not sufficient to det. binding to \*\*\*MHC\*\*\* class I mols., because the majority of motif-contg. peptides failed to bind to the relevant \*\*\*MHC\*\*\*. Finally, specific HLA motifs were used to predict peptide binders of 8, 10, and 11 aa in length. Several high affinity binding peptides were identified for each of the various peptide lengths, indicating a significant size heterogeneity in peptides capable of high affinity binding to HLA-A mols.

L150 ANSWER 5 OF 20 CANCERLIT                      DUPLICATE 1  
 AN 95104310 CANCERLIT  
 TI Identification of a naturally processed HLA A0201-restricted viral peptide from cells expressing human papillomavirus type 16 E6 oncoprotein.  
 AU Bartholomew J S; Stacey S N; Coles B; Burt D J; Arrand J R; Stern P L  
 CS Department of Immunology, Paterson Institute for Cancer Research, Christie Hospital NHS Trust, Manchester, GB.  
 SO Eur J Immunol, (1994). Vol. 24, No. 12, pp. 3175-9.  
 Journal code: EN5. ISSN: 0014-2980.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS MEDL; Cancer Journals; L; Priority Journals  
 LA English  
 OS MEDLINE 95104310  
 EM 9503  
 AB Human papillomavirus ( \*\*\*HPV\*\*\* ) DNA encoding the oncogenic proteins E6 and E7 is usually retained in cervical carcinomas, implicating these proteins as potential target antigens for immune recognition in this virally associated tumor. We have characterized endogenously processed peptides eluted from \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\* \*\*\*I\*\*\* \*\*\*molecules\*\*\* in cells infected with a recombinant vaccinia expressing the \*\*\*HPV\*\*\* -16 E6 oncoprotein. The reverse-phase chromatography profile of peptides eluted from isolated HLA-A0201 molecules in cells expressing the E6 oncoprotein differs from that of cells not expressing E6. Sequential Edman degradation of novel peaks found in the peptide profiles from cells expressing \*\*\*HPV\*\*\* -16 E6 led to the identification of a naturally processed HLA-A0201-restricted E6 peptide of sequence KLPQLCTEL. This approach has allowed the identification of a viral peptide which is processed and presented by cells expressing the E6 oncoprotein and is a likely target for cytotoxic T lymphocyte recognition in HLA-A0201-positive patients.

L150 ANSWER 6 OF 20 CANCERLIT                      DUPLICATE 2  
 AN 94206886 CANCERLIT  
 TI Limitations of predictive motifs revealed by cytotoxic T lymphocyte epitope mapping of the \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* E7 protein.  
 AU Sadovnikova E; Zhu X; Collins S M; Zhou J; Vousden K; Crawford L; Beverley P; Stauss H J  
 CS ICRF Tumour Immunology Unit, University College London Medical School, Courtauld Institute, UK.  
 SO Int Immunol, (1994). Vol. 6, No. 2, pp. 289-96.  
 Journal code: AY5. ISSN: 0953-8178.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS MEDL; L; Priority Journals  
 LA English  
 OS MEDLINE 94206886  
 EM 9406  
 AB \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 16 is found in the majority of cervical cancer patients and the transforming protein E7 is consistently expressed in cancer cells, making it a potential target for immune attack. In this study we have investigated whether E7 gains access to the \*\*\*MHC\*\*\* class I processing pathway and provides cytotoxic T lymphocyte (CTL) stimulating peptide epitopes. CTL were induced in H-2b mice by immunization with recombinant vaccinia virus expressing E7 (Vac-E7). To map CTL recognition, natural peptides were purified from cells expressing either intact or truncated E7 protein. Following peptide separation by HPLC one major CTL epitope was detected and truncated constructs localized this epitope to the C-terminal region. Mapping with synthetic peptides indicated that residues 49-57 (RAHYNIVTF)



were recognised by anti-E7 CTL. Synthetic 49-57 peptide was used to induce CTL, which recognized the same HPLC purified natural peptide fractions as anti-E7 CTL. Binding motifs for H-2b class I molecules did not predict residues 49-57 to be a CTL epitope, but instead the sequence 21-28 (DLYCYEQL) which contains a Kb anchor motif. Synthetic 21-28 peptide was found to bind to Kb class I molecules and readily induced CTL, indicating that the T cell repertoire of H-2b mice can recognize this epitope. However, these CTL did not recognize peptides isolated from E7 expressing cells, showing that natural processing did not produce detectable levels of the 21-28 epitope. Together, the data demonstrate that an unexpected E7 peptide can function as a major CTL epitope.

L150 ANSWER 7 OF 20 CANCERLIT                      DUPLICATE 3  
 AN 94141194 CANCERLIT  
 TI Enzyme immunoassay detection of induction of \*\*\*MHC\*\*\* class I expression by synthetic peptides from the E6 and E7 regions of human papillomavirus type 16.  
 AU Dillner J  
 CS Department of Virology, Karolinska Institute, Stockholm, Sweden.  
 SO J Immunol Methods, (1994). Vol. 167, No. 1-2, pp. 195-205.  
 Journal code: IFE. ISSN: 0022-1759.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS MEDL; Cancer Journals; L; Priority Journals  
 LA English  
 OS MEDLINE 94141194  
 EM 9404  
 AB Viral antigens are presented to cytotoxic T cells (CTL) in the form of endogenously processed peptides bound to \*\*\*major\*\*\*  
 \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* ( \*\*\*MHC\*\*\* )  
 \*\*\*class\*\*\* \*\*\*I\*\*\* \*\*\*molecules\*\*\* . A variety of  
 different methods for measuring the ability of peptides to bind to  
 \*\*\*MHC\*\*\* class I have been described. Several of these methods  
 use the murine lymphoma mutant cell line RMA-S, which has a peptide  
 loading defect resulting in a low expression of surface class I  
 molecules that can be upregulated if a synthetic binding peptide  
 with class I binding ability is added to the culture medium. In  
 order to be able to screen for peptides with \*\*\*MHC\*\*\* class I  
 binding ability, we developed an enzyme immunoassay for quantitation  
 of \*\*\*MHC\*\*\* class I expression on RMA-S cells. 107 synthetic  
 peptides derived from the E6 and E7 regions of human papillomavirus  
 type 16 were screened for ability to upregulate class I expression  
 of Kb or Db alleles. At a concentration of about 300 microM, 9/107  
 peptides were found to restore expression of Db to equal or greater  
 levels than found in the RMA-S parental cell line RMA, while 35/107  
 peptides were able to partially restore Db expression. For Kb,  
 16/107 peptides were able to restore expression and 40/107 peptides  
 induced partial upregulation. Titration experiments showed that  
 upregulation of class I expression by these peptides was dependent  
 on a high peptide concentration, since consistent upregulation could  
 in no case be detected at concentrations below 10 microM. The class  
 I binding peptides identified in the present study may be useful in  
 the study of the CTL response to \*\*\*HPV\*\*\* in mouse model  
 systems. The enzyme immunoassay used could facilitate the rapid  
 search for class I binding peptides.

L150 ANSWER 8 OF 20 MEDLINE  
 AN 95091605 MEDLINE  
 TI Class I \*\*\*MHC\*\*\* -peptide interaction: structural and functional aspects.  
 AU Ruppert J; Kubo R T; Sidney J; Grey H M; Sette A  
 CS Cytel, San Diego, California 92121.  
 NC A118634 (NIAID)  
 SO Behring Inst Mitt, (1994 Jul) (94) 48-60. Ref: 50  
 Journal code: 9KI. ISSN: 0301-0457.  
 CY GERMANY: Germany, Federal Republic of  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 9503  
 AB The structural requirements for the interaction between antigens and class I molecules was investigated through the use of a quantitative assay to measure peptide binding to different \*\*\*MHC\*\*\* class I alleles. We determined the permissiveness of the main anchors reported by Rammensee and his group for peptide binding and defined an extended motif for peptides binding to the HLA-A2.1 allele, including the role of non-anchor positions. It was found that the main anchors were necessary, but not sufficient, for good binding. Certain non-anchor positions contributed significantly to overall



binding and were referred to a secondary anchors. This finding allowed a better prediction of high affinity binding peptides selected from libraries of different viral and tumor proteins. Furthermore, our data allowed correlation of the structural requirements for binding of peptides with crystallographic data of the \*\*\*MHC\*\*\* molecule. In order to characterize allele-specific motifs for a larger number of alleles, the HLA-A alleles A1, A3, A11, and A24, which represent some of the most common alleles found in different ethnic populations, were chosen. Here, most motifs were found to be highly exclusive; however, HLA-A3 and A11 shared a common motif. The defined motifs were validated further by using naturally processed peptides. Those peptides were also synthesized and tested for binding to the appropriate HLA alleles, giving a binding affinity from 0.3 to 200 nM for sequences of naturally processed peptides. Finally, a set of all possible 9-mer peptides from \*\*\*HPV\*\*\* 16 proteins were synthesized and tested for binding to the five class I alleles. For each allele, high affinity binders were identified, thus allowing for selection of possible peptide candidates for a CTL based vaccine.

L150 ANSWER 9 OF 20 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:151455 NLDB  
 TI Peptide Vaccination with a Cytotoxic T-Cell Epitope Derived from the  
 \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\* \*\*\*Virus\*\*\* Type 16 Oncogene  
 E7 Confers Protection Against \*\*\*HPV16\*\*\* -Induced Tumors  
 SO Cancer Weekly, (26 Apr 1993) .  
 ISSN: 0896-7384.  
 PB CW Henderson, Publisher  
 DT Newsletter  
 LA English  
 WC 359

L150 ANSWER 10 OF 20 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:134063 NLDB  
 TI Protection Against a \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\*  
 \*\*\*Virus\*\*\* Type 16 -Induced Tumor by Peptide Vaccination with a  
 Cytotoxic T -Cell Epitope Derived from the Viral Oncogene E7  
 SO Cancer Weekly, (19 Apr 1993) .  
 ISSN: 0896-7384.  
 PB CW Henderson, Publisher  
 DT Newsletter  
 LA English  
 WC 296

L150 ANSWER 11 OF 20 CAPLUS COPYRIGHT 1995 ACS DUPLICATE 4

AN 1994:426884 CAPLUS  
 DN 121:26884  
 TI Peptides of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* for  
 use in \*\*\*human\*\*\* T cell response-inducing compositions  
 IN Kast, Wybe Martin; Melief, Cornelis Joseph Maria; Sette, Alessandro  
 D.; Sidney, John C.  
 PA Rijksuniversiteit Leiden, Neth.  
 SO PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 PI WO 9322338 A1 931111  
 DS W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP,  
 KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK,  
 UA, US, VN  
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR,  
 IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
 AI WO 93-NL93 930504  
 PRAI EP 92-201252 920505  
 EP 92-203870 921210  
 EP 93-200243 930201  
 EP 93-200621 930305  
 DT Patent  
 LA English  
 AB A peptide comprising an \*\*\*amino\*\*\* \*\*\*acid\*\*\* sequence  
 derived from a \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* (\*\*\*HPV\*\*\* ) protein, wherein said \*\*\*amino\*\*\* \*\*\*acid\*\*\* sequence has the ability to bind to a human Major Histocompatibility Complex Class I mol., is claimed. The peptides may be used in prophylactic or therapeutic treatment of cervical carcinoma and other \*\*\*HPV\*\*\* -related diseases (no data). Nine-residue peptides derived from \*\*\*HPV16\*\*\* or \*\*\*HPV18\*\*\* E6 and E7 proteins which bound to HLA-A2.1, -A1, -A2.1, -A3.2, -A11.2, and -A24 mols. were identified.

L150 ANSWER 12 OF 20 USPATFULL



AN 93:89648 USPATFULL  
 TI Covalent polar lipid-peptide conjugates for immunological targeting  
 IN Yatvin, Milton B., Portland, OR, United States  
 Stowell, Michael H. B., Pasadena, CA, United States  
 Malkovsky, Miroslav, Madison, WI, United States  
 PA State of Oregon, Portland, OR, United States (U.S. state government)  
 PI US 5256641 931026  
 AI US 92-911209 920709 (7)  
 RLI Continuation-in-part of Ser. No. US 90-607982, filed on 1 Nov 1990, now patented, Pat. No. US 5149794  
 DT Utility  
 EXNAM Primary Examiner: Rollins, John W.  
 LREP Allegretti & Witcoff, Ltd.  
 CLMN Number of Claims: 23  
 ECL Exemplary Claim: 1  
 GI 7 Drawing Figure(s); 8 Drawing Page(s)  
 LN.CNT 676

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods of facilitating the entry of peptides into cells and targeting such peptides to specific organelles within the cell. The invention provides methods for delivering and specific targeting of antigenically-active peptides to cells for the specific production of immunological reactivity against such peptides, as well as compositions and pharmaceutical compositions of matter comprising such peptides. This invention thereby provides improved methods for vaccine production and in vivo vaccination against pathogenic microorganisms. Methods for alleviating autoimmune disease and ameliorating tissue and organ transplant rejection using such conjugates are also provided.

L150 ANSWER 13 OF 20 CANCERLIT DUPLICATE 5

AN 93233248 CANCERLIT  
 TI Production and characterization of human proliferative T-cell clones specific for human papillomavirus type 1 E4 protein.  
 AU Steele J C; Stankovic T; Gallimore P H  
 CS Department of Cancer Studies, Medical School, University of Birmingham, United Kingdom.  
 SO J Virol, (1993). Vol. 67, No. 5, pp. 2799-806.  
 Journal code: KCV. ISSN: 0022-538X.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS MEDL; Cancer Journals; L; Priority Journals  
 LA English  
 OS MEDLINE 93233248  
 EM 9306

AB Human papillomavirus type 1 (HPV1) virions and E4 protein purified from cutaneous warts were tested in lymphocyte proliferation assays using normal individuals. Both antigens were found to be capable of eliciting good lymphoproliferative responses. Several T-cell clones specific for wart E4 protein were obtained from a donor who had consistently responded very well to E4 in these initial assays. They were maintained in culture by repeated stimulation with antigen and interleukin-2, using an autologous mitomycin-treated lymphoblastoid cell line as a source of antigen-presenting cells. Two of these clones (3F5 and 4A8), which behaved identically, have been studied in more detail. A series of overlapping synthetic peptides covering the entire E1 E4 protein sequence was used to identify a single T-cell epitope which maps to a strongly hydrophilic region spanning \*\*\*amino\*\*\* \*\*\*acid\*\*\* residues 38 to 50. We have also tested the ability of a panel of major histocompatibility complex class II-matched and -mismatched lymphoblastoid cell lines to present this peptide to the T-cell clones in proliferation assays. The study reports that the epitope is restricted through HLA-DQ7 and that it can be recognized by T cells with different T-cell receptor gene rearrangements.

L150 ANSWER 14 OF 20 CANCERLIT DUPLICATE 6

AN 93380495 CANCERLIT  
 TI Vaccination with cytotoxic T lymphocyte epitope-containing peptide protects against a tumor induced by human papillomavirus type 16-transformed cells.  
 AU Feltkamp M C; Smits H L; Vierboom M P; Minnaar R P; de Jongh B M; Drijfhout J W; ter Schegget J; Melief C J; Kast W M  
 CS Department of Immunohematology and Blood bank, University Hospital Leiden, The Netherlands.  
 SO Eur J Immunol, (1993). Vol. 23, No. 9, pp. 2242-9.  
 Journal code: EN5. ISSN: 0014-2980.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 FS MEDL; Cancer Journals; L; Priority Journals  
 LA English



OS MEDLINE 93380495

EM 9311

AB Cytotoxic T lymphocyte (CTL) peptide epitopes can be used for immunization of mice against lethal virus infection. To study whether this approach can be successful against virus-induced tumors we generated a B6 (H-2b) tumorigenic cell line transformed by \*\*\*human\*\*\* \*\*\*papillomavirus\*\*\* ( \*\*\*HPV\*\*\* ). This \*\*\*virus\*\*\* is detected in over 90% of all human cervical cancers. To identify vaccine candidates, we generated a set of 240 overlapping peptides derived from the \*\*\*HPV\*\*\* type 16 ( \*\*\*HPV16\*\*\* ) oncogenes E6 and E7. These peptides were tested for their ability to bind H-2Kb and H-2Db \*\*\*MHC\*\*\* class I molecules. Binding peptides were compared with the presently known peptide-binding motifs for H-2Kb and H-2Db and the predictive value of these motifs is shortly discussed. The high-affinity H-2Db-binding peptide and putative CTL epitope E7 49-57 (RAHYNIVTF) was used in vaccination studies against \*\*\*HPV\*\*\* 16-transformed tumor cells. Immunization with peptide E7 49-57 rendered mice insensitive to a subsequent challenge with \*\*\*HPV\*\*\* 16-transformed tumor cells in vivo, and induced a CTL response which lysed the tumor cells in vitro.

L150 ANSWER 15 OF 20 CANCERLIT DUPLICATE 7

AN 93329139 CANCERLIT

TI Relation between skin cancer, humoral responses to human papillomaviruses, and HLA class II molecules in renal transplant recipients.

AU Bavincq J N; Gissmann L; Claas F H; Van der Woude F J; Persijn G G; Ter Schegget J; Vermeer B J; Jochmus I; Muller M; Steger G; et al

CS Department of Dermatology, University Hospital, Leiden, The Netherlands.

SO J Immunol, (1993). Vol. 151, No. 3, pp. 1579-86.  
Journal code: IFB. ISSN: 0022-1767.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals

LA English

OS MEDLINE 93329139

EM 9309

AB Human papillomaviruses ( \*\*\*HPV\*\*\* ), especially the epidermodysplasia verruciformis (EV)-associated \*\*\*HPV\*\*\* 5, 8, 14, 17, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. \*\*\*MHC\*\*\* class I and class II genes are involved in the cellular immune response to viral and tumor Ag. Little is known about humoral responses to \*\*\*HPV\*\*\* in recipients with and without skin cancer. We investigated the prevalence of antibodies to the early (E) protein E7 and the major capsid late (L) protein L1 of \*\*\*HPV\*\*\* 8. In addition, we studied the association of HLA class II molecules with these antibody responses. The E7 and L1 open reading frames of \*\*\*HPV\*\*\* 8 were bacterially expressed as beta-galactosidase fusion proteins, which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to \*\*\*HPV\*\*\* 8 E7 and L1, by Western blot analysis. The detection of anti- \*\*\*HPV\*\*\* 8 L1 antibodies represents the immune response to \*\*\*HPV\*\*\* 8 and possibly other EV-associated \*\*\*HPV\*\*\* , because cross-reactivity between the representatives of this \*\*\*HPV\*\*\* subgenus can occur. The antibody responses to HLA Ag were used as controls. Recipients who had IgM antibodies but no IgG antibodies to L1 of \*\*\*HPV\*\*\* 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies (patients with an apparently good humoral response to L1 of \*\*\*HPV\*\*\* 8) had skin cancer in only 18% of cases. The estimated relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5 (95% confidence interval, 1.1 to 18.1). We found no association between the antibody response to HLA Ag and the occurrence of skin cancer. A strong linkage between the absent class switch of antibody production in response to L1 of \*\*\*HPV\*\*\* 8 and HLA-DR7 was observed (relative risk, 26.2). Renal transplant recipients who have no apparent class switch from IgM to IgG production in response to Ag encoded by L1 of \*\*\*HPV\*\*\* 8 or possibly other EV-associated \*\*\*HPV\*\*\* are at an increased risk of skin cancer. The association with HLA-DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the \*\*\*MHC\*\*\* .

L150 ANSWER 16 OF 20 CAPLUS COPYRIGHT 1995 ACS

AN 1992:590111 CAPLUS

DN 117:190111



TI \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* peptides and  
organisms producing said peptides for use in vaccine compositions  
IN Thomas, Elaine Kinney; Chen, Lieping; Blake, James; Hellstrom, Karl  
Erik; Hellstrom, Ingegerd; Hu, Shiu Lok  
PA Bristol-Myers Squibb Co., USA  
SO PCT Int. Appl., 82 pp.  
CODEN: PIXXD2  
PI WO 9205248 A1 920402  
DS W: AU, CA, JP, KR, NO  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE  
AI WO 91-US7081 910926  
PRAI US 90-588384 900926  
DT Patent  
LA English

AB Immunogenic peptides corresponding to peptides expressed in  
mammalian cells in response to \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
\*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) infection are described. Recombinant  
organisms (such as vaccinia virus or tumor cells) producing such a  
peptide, or the peptide, can be used to treat \*\*\*HPV\*\*\*  
infections. Recombinant vaccinia virus expressing either the  
\*\*\*HPV\*\*\* E7 or E8 gene, and mammalian cell expression plasmids  
contg. these genes, were prepd. Mice were injected i.p. with  
\*\*\*HPV\*\*\* E7 epitope-producing fibroblasts, then challenged by  
s.c. administration of a tumorigenic dose of M2 melanoma cells  
transfected with \*\*\*HPV16\*\*\* E7 expression vector. A transient  
development of tumors followed by tumor regression was obsd.

L150 ANSWER 17 OF 20 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 8  
AN 92:501950 BIOSIS

DN BA94:120475  
TI INDUCTION OF CYTOTOXIC T LYMPHOCYTES WITH PEPTIDES IN-VITRO  
IDENTIFICATION OF CANDIDATE T-CELL EPITOPES IN \*\*\*HUMAN\*\*\*  
\*\*\*PAPILLOMA\*\*\* \*\*\*VIRUS\*\*\*

AU STAUSS H J; DAVIES H; SADOVNIKOVA E; CHAIN B; HOROWITZ N; SINCLAIR C  
CS IMP. CANCER RES. FUND, HUM. TUM. IMMUNOL. GROUP, UNIVERSITY COLL.,  
MIDDLESEX HOSP., LONDON W1P 8BT, UK.  
SO PROC NATL ACAD SCI U S A 89 (17). 1992. 7871-7875. CODEN: PNASA6  
ISSN: 0027-8424

LA English

AB A set of overlapping peptides corresponding to the L1, E6, and E7  
proteins of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* 16  
was tested for their ability to bind to \*\*\*major\*\*\*  
\*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\*  
\*\*\*I\*\*\* \*\*\*molecules\*\*\* and to stimulate cytotoxic T-lymphocyte  
(CTL) responses in vitro. A class I binding assay using intact RMA-S  
cells showed that 20 of the 99 \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
\*\*\*virus\*\*\* peptides bound to H-2Kb and/or Db molecules. Fifteen of  
the 20 class I-binding peptides stimulated primary CTL responses,  
whereas peptides that were negative in the binding assay failed to do  
so. Peptide-induced CTLs recognized the immunizing peptide very  
efficiently, requiring no more than 1-10 nM peptide for target cell  
lysis. However, two observations were made that have important  
implications for the design of peptide-based vaccines for inducing  
CTLs. (i) Not all major histocompatibility complex-binding peptides  
that contained known motifs characteristic of naturally processed  
peptides induced CTLs. (ii) The efficiency of CTL lysis was strongly  
decreased when the size of the target peptide differed by only one  
\*\*\*amino\*\*\* \*\*\*acid\*\*\* residue from that of the immunizing  
peptide. We conclude that peptides chosen for vaccination must  
correspond in length to naturally processed peptides.

L150 ANSWER 18 OF 20 CANCERLIT DUPLICATE 9

AN 92273283 CANCERLIT  
TI DEFINITION OF IMMUNOGENIC DETERMINANTS OF THE HUMAN PAPILLOMAVIRUS  
TYPE 16 NUCLEOPROTEIN E7.

AU Altmann A; Jochmus-Kudielka I; Frank R; Gausepohl H; Moebius U;  
Gissmann L; Meuer S C  
CS Department of Applied Immunology, German Cancer Research Centre,  
Heidelberg.

SO Eur J Cancer, (1992). Vol. 28, No. 2-3, pp. 326-33.  
Journal code: ARV. ISSN: 0959-8049.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; L; Priority Journals

LA English

OS MEDLINE 92273283

EM 9208

AB Specific T lymphocyte lines and T cell clones were established from  
peripheral blood mononuclear cells of asymptomatic seropositive  
individuals employing synthetic peptides which correspond to the  
sequence of the human papillomavirus ( \*\*\*HPV\*\*\* ) type 16  
transforming protein E7. Specificity analysis of T cells as



determined by means of [3H] thymidine incorporation after stimulation with individual peptides revealed three immunogenic determinants of E7 that are recognised in association with at least two different HLA haplotypes. One N-terminal region (aminoacids 5-18) was recognised by one T cell line. T cell clones and the corresponding T cell line established from another donor responded to a different N-terminal (17-38) and to a C-terminal region (69-86). The N-terminal sequence 5-18 and the C-terminal determinant contain a periodicity of hydrophilic and hydrophobic residues that have been found in many T cell epitopes. Phenotypic characterisation of T cell clones by indirect immunofluorescence revealed that the T cell clones expressed the CD4 surface glycoprotein suggesting that the specific E7 determinants were recognised in association with major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II molecules. With regard to functional properties, at least three T cell clones exhibited specific cytotoxic activity towards autologous B lymphocytes transformed by Epstein-Barr virus in the presence of the relevant \*\*\*HPV16\*\*\* E7 peptides. The implications of these results regarding the development of vaccination strategies and host-virus interaction are discussed.

L150 ANSWER 19 OF 20 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 10

AN 91:181239 BIOSIS

DN BA91:95988

TI THE INDUCTION OF CYTOTOXIC T-LYMPHOCYTE PRECURSOR CELLS BY RECOMBINANT VACCINIA \*\*\*VIRUS\*\*\* EXPRESSION \*\*\*HUMAN\*\*\* \*\*\*PAPILLOMAVIRUS\*\*\* TYPE 16 L1.

AU ZHOU J; MCINDOE A; DAVIES H; SUN X-Y; CRAWFORD L

CS ICRF TUMOUR VIRUS GROUP, DEP. PATHOL., UNIV. CAMBRIDGE, TENNIS COURT ROAD, CAMBRIDGE CB2 1QP, UK.

SO VIROLOGY 181 (1). 1991. 203-210. CODEN: VIRLAX ISSN: 0042-6822

LA English

AB Expression of the major coat protein L1 of \*\*\*human\*\*\*

\*\*\*papillomavirus\*\*\* type 16 by recombinant vaccinia

\*\*\*viruses\*\*\* using a vaccinia late promoter and their use in generating antibodies have already been reported (Zhou et al., 1990). We have now constructed recombinant vaccinia viruses (VVs) which express the L1 protein from an early promoter with the intention of inducing cell-mediated immunity. This necessitated the removal of sequence motifs (TTTTNT) from the L1 gene which would otherwise have caused transcription termination when expressed from a vaccinia virus early promoter. The nucleotide sequence was mutated to retain the correct \*\*\*amino\*\*\* \*\*\*acid\*\*\* sequence of the L1 protein.

Full-length mRNA and L1 protein were generated in cells infected with the recombinant virus containing the mutant sequence, whereas the wild-type sequence generated only truncated mRNA and no detectable protein. Mice were immunized with VV expressing L1 from the mutant sequence and from the wild-type sequence in constructs with either early or late vaccinia virus promoters. Only the early promoter construct were effective in priming cytotoxic T lymphocytes (CTL). Moreover the mutant sequence was significantly more effective than the wild-type sequence. The same L1 sequences, expressed from a vaccinia virus late promoter or coexpressed with \*\*\*MHC\*\*\* Class I molecules also expressed from a late promoter, produced high levels of L1 protein in both cases but nevertheless failed to elicit CTL activity. This is the first report of an \*\*\*HPV\*\*\* -specific CTL response and we have reaffirmed the importance of choosing the correct promoter and sequence expressed when using recombinant vaccinia viruses to induce cytotoxic T lymphocytes. These data are relevant for the design of vaccines to generate cell-mediated immunity against human papillomavirus infection.

L150 ANSWER 20 OF 20 CANCERLIT DUPLICATE 11

AN 91073131 CANCERLIT

TI DEFINITION OF MURINE T HELPER CELL DETERMINANTS IN THE MAJOR CAPSID PROTEIN OF HUMAN PAPILLOMAVIRUS TYPE 16.

AU Davies D H; Hill C M; Rothbard J B; Chain B M

CS Department of Biology, University College London, U.K.

SO J Gen Virol, (1990). Vol. 71, Pt. 11, pp. 2691-8.

Journal code: I9B. ISSN: 0022-1317.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals

LA English

OS MEDLINE 91073131

EM 9102

AB Three murine major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II-restricted T cell determinants were identified in the major capsid protein L1 of human papillomavirus ( \*\*\*HPV\*\*\* ) type 16. Peptides derived from \*\*\*HPV\*\*\* -16 L1, which contain putative T cell epitopes located by a predictive algorithm, were synthesized and tested for lymphoproliferative activity by direct immunization,



followed by in vitro assay of responses to peptides or recombinant \*\*\*HPV\*\*\* -16 L1. The \*\*\*MHC\*\*\* restriction of the stimulatory peptides was determined using blocking monoclonal antibodies against class II molecules. The responses, which were specific for the priming peptides alone, cross-reacted with recombinant L1 but not with analogous peptides derived from other \*\*\*HPV\*\*\* types.

=> s l111 and peptid?

TOTAL FOR ALL FILES

L187 81 L111 AND PEPTID?

=> dup rem l187

DUPLICATE IS NOT AVAILABLE IN 'DRUGLAUNCH'. ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE  
PROCESSING COMPLETED FOR L187

L188 31 DUP REM L187 (50 DUPLICATES REMOVED)

=> d bib ab 1-31

L188 ANSWER 1 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:426198 NLDB

TI Drug Development/Cancer Vaccines "Development of Vaccine and Immunotherapeutic Strategies for \*\*\*HPV\*\*\* Related Cervical Carcinoma." T.-C. Wu and D.M. Pardoll. Johns Hopkins Medical Institutions, Baltimore, Maryland.

SO Vaccine Weekly, (16 Jan 1995) .  
ISSN: 1074-2921.

PB Charles W Henderson  
DT Newsletter  
LA English  
WC 416

L188 ANSWER 2 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:513920 NLDB

TI Human Papillomavirus \*\*\*Peptide\*\*\* Engineering Allows Vaccination Against \*\*\*HPV\*\*\*

SO Vaccine Weekly, (27 Mar 1995) .  
ISSN: 1074-2921.

PB Charles W Henderson  
DT Newsletter  
LA English  
WC 453

L188 ANSWER 3 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 95:23020 NLDB

TI Cytel Emphasizes New Targets

SO Applied Genetics News, (Jun 1995) Vol. 15, No. 10.  
ISSN: 0271-7107.

PB Business Communications Company, Inc  
DT Newsletter  
LA English  
WC 323

L188 ANSWER 4 OF 31 CAPLUS COPYRIGHT 1995 ACS

AN 1995:442210 CAPLUS

DN 122:211608

TI Molecular mimicry in T cell-mediated autoimmunity: viral \*\*\*peptides\*\*\* activate human T cell clones specific for myelin basic protein

AU Wucherpfennig, Kai W.; Strominger, Jack L.

CS Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA

SO Cell (Cambridge, Mass.) (1995), 80(5), 695-705  
CODEN: CELLB5; ISSN: 0092-8674

DT Journal  
LA English

AB Structural similarity between viral T cell epitopes and self-\*\*\*peptides\*\*\* could lead to the induction of an autoaggressive T cell response. Based on the structural requirements for both \*\*\*MHC\*\*\* class II binding and TCR recognition of an immunodominant myelin basic protein (MBP) \*\*\*peptide\*\*\*, criteria for a data search were developed in which the degeneracy of amino acid side chains required for \*\*\*MHC\*\*\* class II binding and the conservation of those required for T cell activation were considered. A panel of 129 \*\*\*peptides\*\*\* that matched the mol. mimicry motif was tested on seven MBP-specific T cell clones from



multiple sclerosis patients. Seven viral and one bacterial  
\*\*\*peptide\*\*\* efficiently activated three of these clones. Only  
one \*\*\*peptide\*\*\* could have been identified as a mol. mimic by  
sequence alignment. The observation that a single T cell receptor  
can recognize quite distinct but structurally related  
\*\*\*peptides\*\*\* from multiple pathogens has important implications  
for understanding the pathogenesis of autoimmunity.

L188 ANSWER 5 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 1

AN 95:157688 BIOSIS

DN 98171988

TI \*\*\*Peptide\*\*\* engineering allows cytotoxic T-cell vaccination  
against \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* tumour  
antigen, E6.

AU Lipford G B; Bauer S; Wagner H; Heeg K

CS Inst. Med. Microbiol., Tech. Univ. Munich, Trogerstr. 9, Munich  
81675, Germany

SO Immunology 84 (2). 1995. 298-303. ISSN: 0019-2805

LA English

AB Major histocompatibility complex ( \*\*\*MHC\*\*\* ) class I  
allele-specific binding motifs have proved useful in predicting  
cytotoxic T-cell epitopes from immunogenic proteins. In a search of  
the E6 protein from \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\*  
type 16 utilizing the K-b binding motif, we discovered four potential  
binding \*\*\*peptides\*\*\*. One \*\*\*peptide\*\*\*, E6.1 (sequence  
50-57, YDFAFRDL), was poor in its ability to stabilize empty K-b on  
RMA-S cells, with a t-1/2 = 33 min versus 30 min for empty K-b. This  
\*\*\*peptide\*\*\* subsequently proved to be non-immunogenic upon mouse  
in vivo vaccination. It was hypothesized that an isoleucine for  
aspartate substitution at position 2 would improve K-b stabilization  
kinetics and therefore immunogenic potential. The engineered  
\*\*\*peptide\*\*\* E6.1 I2 increased the K-b t-1/2 to 100 min and was  
immunogenic upon in vivo vaccination. Cytolytic T lymphocytes (CTL)  
raised with the E6.1 I2 \*\*\*peptide\*\*\* responded to cells pulsed  
with either the wild-type \*\*\*peptide\*\*\* or the engineered  
\*\*\*peptide\*\*\*, implying a blindness to the substitution. More  
striking, these CTL also lysed a syngeneic cell line transfected with  
the E6 gene, implying that the E6.1 \*\*\*peptide\*\*\* was processed  
and presented. These data demonstrate that subimmunogenic  
\*\*\*peptides\*\*\* can be engineered to improve binding kinetics, which  
in turn improves immunogenicity. Provided that poor binding  
\*\*\*peptides\*\*\* are processed, the induction threshold for CTL  
activation can be achieved with engineered \*\*\*peptides\*\*\*, thus  
allowing for the kill of wild-type target cells. This approach may  
prove relevant to the design of subunit vaccines to vitally induced  
tumours.

L188 ANSWER 6 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:389594 NLDB

TI Biotechnology - Vaccine Engineering: "New Strategies in Vaccine  
Engineering." D.M. Pardoll. Johns Hopkins University School of  
Medicine.

SO Vaccine Weekly, (5 Dec 1994) .

ISSN: 1074-2921.

PB Charles W Henderson

DT Newsletter

LA English

WC 795

L188 ANSWER 7 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 94:44272 NLDB

TI Encouraging Developments

SO Antiviral Agents Bulletin, (Jan 1994) Vol. 7, No. 1.

ISSN: 0897-9871.

PB Biotechnology Information Institute

DT Newsletter

LA English

WC 2661

L188 ANSWER 8 OF 31 COPYRIGHT 1995 PJB

AN 94:17778 PHIN

DN S00420996

DED 22 Nov 1994

TI British Technology Group (BTG) seeks new development capital

SO Scrip (1994) No. 1977 p16

DT Newsletter

FS FULL



L188 ANSWER 9 OF 31 CAPLUS COPYRIGHT 1995 ACS  
 AN 1994:455887 CAPLUS  
 DN 121:55887  
 TI Antigenic \*\*\*peptides\*\*\* binding class I \*\*\*MHC\*\*\* proteins  
 and their diagnostic and therapeutic uses  
 IN Kubo, Ralph T.; Grey, Howard M.; Sette, Alessandro; Celis, Esteban  
 PA Cytel Corp., USA  
 SO PCT Int. Appl., 149 pp.  
 CODEN: PIXXD2  
 PI WO 9403205 A1 940217  
 DS W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP,  
 KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD,  
 SE, SK, UA, VN  
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR,  
 IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
 AI WO 93-US7421 930806  
 PRAI US 92-926666 920807  
 US 93-27746 930305  
 DT Patent  
 LA English  
 AB Antigenic \*\*\*peptides\*\*\* capable of specifically binding  
 selected \*\*\*MHC\*\*\* antigens and inducing T cell activation in T  
 cells restricted by the corresponding \*\*\*MHC\*\*\* allele are  
 described. The \*\*\*peptides\*\*\* are used to elicit an immune  
 response against a desired antigen. HLA-A antigens were purified by  
 affinity chromatog. against allele-specific or monoclonal  
 antibodies. \*\*\*Peptides\*\*\* remaining bound to the HLA-A  
 antigens after affinity purifn. were eluted at acidic pH,  
 fractionated by HPLC and individual fractions immobilized and  
 sequenced. Residues essential for binding to the antigen were  
 detected during sequencing were obsd. in complex fractions by being  
 the major amino acid in a given cycle of the sequencing reaction. A  
 decapeptide specific for an HLA-A3.2 antigen was obsd. with position  
 2 V, L; or M, position 3 Y or D; position 7 I; position 8 Q or N;  
 and positions 9 and 10 both K. Similarly, motifs were obsd. for  
 HLA-A1, A11, and A24.1. Antigens contg. these motifs were searched  
 for in sequence databases and a no. of such sequences were found in  
 tumor-specific antigens and viral proteins. These \*\*\*peptides\*\*\*  
 were used as probes for the assay of the cognate HLA-A antigens.

L188 ANSWER 10 OF 31 WPIDS COPYRIGHT 1995 DERWENT INFORMATION LTD  
 AN 94-035970 [05] WPIDS  
 DNC C94-016558  
 TI Monoclonal antibodies for diagnosis or therapy - directed against  
 conjugate of \*\*\*MHC\*\*\* class I mol and \*\*\*peptide\*\*\*  
 antigen.  
 DC B04 D18  
 IN HAEMMERLING, G  
 PA (DEKR-N) DEUT KREBSFORSCHUNGSZENTRUM  
 CYC 1  
 PI DE 4224542 A1 940127 (9405)\* 3 pp  
 ADT DE 4224542 A1 DE 92-4224542 920724  
 PRAI DE 92-4224542 920724  
 AB DE 4224542 A UPAB: 940315  
 Producing monoclonal antibodies directed against a conjugate of a  
 major histocompatibility complex class I mol. (I) and a  
 \*\*\*peptide\*\*\* antigen (II) comprises (a) isolating (I); (b)  
 inserting a (I)-encoding gene into the genome of a mouse to permit  
 expression of the gene; (c) conjugating (I) with (II); (d)  
 immunising the transformed mouse with the conjugate; (e) isolating  
 spleen cells from the mouse; and (f) producing and opt. humanising  
 monoclonal antibodies in known manner.  
 Process (I) may be isolated from CS7 AL/6 mouse RMA-S tumour  
 cells or human EBV transformed cells, or may be isolated from  
 tissue, or may be produced by recombinant DNA techniques. Step (b)  
 may be omitted if (I) was isolated from the same mouse strain as  
 that to be immunised. (II) may be a viral or tumour antigen, e.g.,  
 the human melanoma antigen MAGE-1 or the tumour antigen produced by  
 the \*\*\*HPV\*\*\* E6 or E7 oncogene.  
 USE - The antibodies are useful for diagnosis and therapy of  
 tumours and infections, e.g., as a substitute for tumour-specific  
 cytotoxic T cells.  
 Dwg. 0/0

L188 ANSWER 11 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS  
 AN 95:1473 BIOSIS  
 DN 98015773  
 TI \*\*\*HPV\*\*\* 18-derived synthetic \*\*\*peptides\*\*\* with ability to  
 upregulate \*\*\*MHC\*\*\* class I expression on RMA-S or T2 cells, as  
 detected by enzyme immunoassay.  
 AU Dillner J



CS Dep. Virology, Karolinska Inst., Stockholm, Sweden  
SO Stanley, M. A. (Ed.). Immunology of human papillomaviruses; Second International Workshop on HPV Immunology, Cambridge, England, UK, July 5-7, 1993. xi+332p. Plenum Press: New York, New York, USA; London, England, UK. 0 (0). 1994. 201-205. ISBN: 0-306-44714-2  
DT Book; Conference  
LA English

L188 ANSWER 12 OF 31 CAPLUS COPYRIGHT 1995 ACS

AN 1995:8346 CAPLUS

DN 122:7346

TI Role of HLA-A motifs in identification of potential CTL epitopes in human papillomavirus type 16 E6 and E7 proteins

AU Kast, W. Martin; Brandt, Remco M. P.; Sidney, John; Drijfhout, Jan Wouter; Kubo, Ralph T.; Grey, Howard M.; Melief, Cornelis J. M.; Sette, Alessandro

CS Dep. Immunohematol., Univ. Hosp., Leiden, Neth.

SO J. Immunol. (1994), 152(8), 3904-12

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The authors have measured the binding affinity for five HLA-A alleles: HLA-A1 (A\*0101), A2.1 (A\*0201), A3 (A\*0301), A11 (A\*1101), and A24 (A\*2401); of a set of all possible nonamer \*\*\*peptides\*\*\* of human papillomavirus type 16 E6 and E7 proteins. High affinity binding \*\*\*peptides\*\*\* were identified for each of the alleles, thus allowing the authors to select several candidates for CTL-based vaccines. Moreover, this unbiased set of \*\*\*peptides\*\*\* allowed an evaln. of the predictive value of HLA motifs derived either from the anal. of sequencing of pools of naturally processed \*\*\*peptides\*\*\* or from the binding anal. of polyalanine nonameric \*\*\*peptides\*\*\* that differed in the amino acids (aa) present at the anchor positions. Whereas pool sequence-derived motifs were present in only 27% of high affinity binders, the more expanded motif, based on anal. of different aa substitutions at the anchor positions, was present in 73% of high affinity binders. Furthermore, it was found that the presence of anchor residues in a \*\*\*peptide\*\*\* was in itself not sufficient to det. binding to \*\*\*MHC\*\*\* class I mols., because the majority of motif-contg. \*\*\*peptides\*\*\* failed to bind to the relevant \*\*\*MHC\*\*\*. Finally, specific HLA motifs were used to predict \*\*\*peptide\*\*\* binders of 8, 10, and 11 aa in length. Several high affinity binding \*\*\*peptides\*\*\* were identified for each of the various \*\*\*peptide\*\*\* lengths, indicating a significant size heterogeneity in \*\*\*peptides\*\*\* capable of high affinity binding to HLA-A mols.

L188 ANSWER 13 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 2

AN 95:80678 BIOSIS

DN 98094978

TI Identification of a naturally processed HLA A0201-restricted viral \*\*\*peptide\*\*\* from cells expressing human papillomavirus type 16 E6 oncoprotein.

AU Bartholomew J S; Stacey S N; Coles B; Burt D J; Arrand J R; Stern P L

CS Dep. Immunol., Cancer Res. Campaign Lab., Paterson Inst. Cancer Res.,

Christie Hosp. NHS Trust, Wilmslow Road, Manchester M20 9BX, UK

SO European Journal of Immunology 24 (12). 1994. 3175-3179. ISSN:

0014-2980

LA English

AB Human papillomavirus (HPV) DNA encoding the oncogenic proteins E6 and E7 is usually retained in cervical carcinomas, implicating these proteins as potential target antigens for immune recognition in this virally associated tumor. We have characterized endogenously processed \*\*\*peptides\*\*\* eluted from \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\* \*\*\*molecules\*\*\* in cells infected with a recombinant vaccinia expressing the \*\*\*HPV\*\*\* -16 E6 oncoprotein. The reverse-phase chromatography profile of \*\*\*peptides\*\*\* eluted from isolated HLA-A0201 molecules in cells expressing the E6 oncoprotein differs from that of cells not expressing E6. Sequential Edman degradation of novel peaks found in the \*\*\*peptide\*\*\* profiles from cells expressing \*\*\*HPV\*\*\* -16 E6 led to the identification of a naturally processed HLA-A0201-restricted E6 \*\*\*peptide\*\*\* of sequence KLPQLCTEL. This approach has allowed the identification of a viral \*\*\*peptide\*\*\* which is processed and presented by cells expressing the E6 oncoprotein and is a likely target for cytotoxic T lymphocyte recognition in HLA-A0201-positive patients.

L188 ANSWER 14 OF 31 SCISEARCH COPYRIGHT 1995 ISI (R)

AN 94:579067 SCISEARCH



GA The Genuine Article (R) Number: PF475  
 TI DQA1 AND DQB1 GENES IN PATIENTS WITH SQUAMOUS-CELL CARCINOMA OF THE  
 CERVIX - RELATIONSHIP TO HUMAN PAPILLOMAVIRUS INFECTION AND  
 PROGNOSIS  
 AU HELLAND A; BORRESEN A L (Reprint); KRISTENSEN G; RONNINGEN K S  
 CS NORWEGIAN RADIUM HOSP, INST CANC RES, DEPT GENET, ULLERNCHAUSSEAN  
 70, N-0310 OSLO, NORWAY (Reprint); NORWEGIAN RADIUM HOSP, INST CANC  
 RES, DEPT GENET, ULLERNCHAUSSEAN 70, N-0310 OSLO, NORWAY; NORWEGIAN  
 RADIUM HOSP, INST CANC RES, DEPT GENET, N-0310 OSLO, NORWAY; NATL  
 HOSP, INST TRANSPLANTAT IMMUNOL, N-0027 OSLO, NORWAY  
 CYA NORWAY  
 SO CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION, (SEP 1994) Vol. 3, No.  
 6, pp. 479-486.  
 ISSN: 1055-9965.  
 DT Article; Journal  
 FS CLIN  
 LA ENGLISH  
 REC Reference Count: 60

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB Women carrying serological HLA-DQ3 specificity have previously  
 been found to have an increased risk of developing squamous cell  
 carcinoma of the cervix. Here we report the distribution of DQA1  
 and DQB1 genes in 158 Norwegian patients with squamous cell  
 carcinoma of the cervix and in 186 ethnically matched controls. The  
 DQA1 typing revealed an increase of the DQA1\*030X allele among the  
 patients compared to the controls [odds ratio (OR) = 1.77] and a  
 decreased frequency of DQA1\*0201 among the patients (OR = 0.57).  
 DQB1\*0301 was increased (OR = 1.81) and DQB1\*0201 was decreased (OR  
 = 0.64) among the patients compared to the controls. Among the  
 patients, 67% carried genes encoding DQ3 (DQB1\*0301, DQB1\*0302, or  
 DQB1\*0303) compared to 51% of the controls, which gives an odds  
 ratio of 2.0, significant both in corrected and uncorrected  
 statistical analysis. The haplotype DQA1\*0201-DQB1\*0201 was  
 decreased among the patients compared to the controls (OR = 0.38).  
 Human papillomavirus ( \*\*\*HPV\*\*\* ) has been demonstrated to be a  
 contributing factor in the development of this carcinoma. Primary  
 tumors (fresh frozen) from 65 of the patients were analyzed for the  
 presence of \*\*\*HPV\*\*\* 16 and \*\*\*HPV\*\*\* 18 by polymerase  
 chain reaction. The DQA1-DQB1 haplotypes were distributed randomly  
 among the patients with \*\*\*HPV\*\*\* 16 or \*\*\*HPV\*\*\* 18 present  
 in their tumors so no association was found. Neither was there any  
 difference between DQ3-positive and DQ3-negative patients in the  
 frequency of \*\*\*HPV\*\*\* 16-or \*\*\*HPV\*\*\* 18-positive tumors.  
 DQB1\*03 showed no independent significant association with  
 relapse-free survival. However, the patients positive for  
 DQB1\*0301, DQB1\*0302, or DQB1\*0303 and DQA1\*030X turned out to have  
 a worse prognosis, both in the univariate (P = 0.0057) and  
 multivariate (P = 0.0493) analyses.

L188 ANSWER 15 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 3  
 AN 94:160183 BIOSIS  
 DN 97173183

TI Limitations of predictive motifs revealed by cytotoxic T lymphocyte  
 epitope mapping of the \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
 \*\*\*virus\*\*\* E7 protein.  
 AU Sadvnikova E; Zhu X; Collins S M; Zhou J; Vousden K; Crawford L;  
 Beverley P; Stauss H J  
 CS ICRF Tumour Immunol. Unit, Univ. Coll. London Med. Sch., Courtauld  
 Inst., 91 Riding House St., London W1P 8BT, UK  
 SO International Immunology 6 (2). 1994. 289-296. ISSN: 0953-8178  
 LA English  
 AB \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* )  
 type 16 is found in the majority of cervical cancer patients and the  
 transforming protein E7 is consistently expressed in cancer cells,  
 making it a potential target for immune attack. In this study we have  
 investigated whether E7 gains access to the \*\*\*MHC\*\*\* class I  
 processing pathway and provides cytotoxic T lymphocyte (CTL)  
 stimulating \*\*\*peptide\*\*\* epitopes. CTL were induced in H-2-b  
 mice by immunization with recombinant vaccinia virus expressing E7  
 (Vac-E7). To map CTL recognition, natural \*\*\*peptides\*\*\* were  
 purified from cells expressing either intact or truncated E7 protein.  
 Following \*\*\*peptide\*\*\* separation by HPLC one major CTL epitope  
 was detected and truncated constructs localized this epitope to the  
 C-terminal region. Mapping with synthetic \*\*\*peptides\*\*\*  
 indicated that residues 49 - 57 (RAHYNIVTF) were recognised by  
 anti-E7 CTL. Synthetic 49 - 57 \*\*\*peptide\*\*\* was used to induce  
 CTL, which recognized the same HPLC purified natural \*\*\*peptide\*\*\*  
 fractions as anti-E7 CTL. Binding motifs for H-2-b class I molecules  
 did not predict residues 49 - 57 to be a CTL epitope, but instead the  
 sequence 21 - 28 (DLYCYEQL) which contains a Kb anchor motif.  
 Synthetic 21 -28 \*\*\*peptide\*\*\* was found to bind to K-b Class I



molecules and readily induced CTL, indicating that the T cell repertoire of H-2-b mice can recognize this epitope. However, these CTL did not recognize \*\*\*peptides\*\*\* isolated from E7 expressing cells, showing that natural processing did not produce detectable levels of the 21 - 28 epitope. Together, the data demonstrate that an unexpected E7 \*\*\*peptide\*\*\* can function as a major CTL epitope.

L188 ANSWER 16 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 4

AN 94:226091 BIOSIS

DN 97239091

TI Enzyme immunoassay detection of induction of \*\*\*MHC\*\*\* class I expression by synthetic \*\*\*peptides\*\*\* from the E6 and E7 regions of human papillomavirus type 16.

AU Dillner J

CS Dep. Virol., Karolinska Inst., SBL, S-10521 Stockholm, SWE

SO Journal of Immunological Methods 167 (1-2). 1994. 195-205. ISSN: 0022-1759

LA English

AB Viral antigens are presented to cytotoxic T cells (CTL) in the form of endogenously processed \*\*\*peptides\*\*\* bound to \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* ( \*\*\*MHC\*\*\* ). \*\*\*class\*\*\* \*\*\*I\*\*\* \*\*\*molecules\*\*\* . A variety of different methods for measuring the ability of \*\*\*peptides\*\*\* to bind to \*\*\*MHC\*\*\* class I have been described. Several of these methods use the murine lymphoma mutant cell line RMA-S, which has a \*\*\*peptide\*\*\* loading defect resulting in a low expression of surface class I molecules that can be upregulated if a synthetic binding \*\*\*peptide\*\*\* with class I binding ability is added to the culture medium. In order to be able to screen for \*\*\*peptides\*\*\* with \*\*\*MHC\*\*\* class I binding ability, we developed an enzyme immunoassay for quantitation of \*\*\*MHC\*\*\* class I expression on RMA-S cells. 107 synthetic \*\*\*peptides\*\*\* derived from the E6 and E7 regions of human papillomavirus type 16 were screened for ability to upregulate class I expression of K-b or D-b alleles. At a concentration of about 300 mu-M, 9/107 \*\*\*peptides\*\*\* were found to restore expression of D-b to equal or greater levels than found in the RMA-S parental cell line RMA, while 35/107 \*\*\*peptides\*\*\* were able to partially restore D-b expression. For K-b, 16/107 \*\*\*peptides\*\*\* were able to restore expression and 40/107 \*\*\*peptides\*\*\* induced partial upregulation. Titration experiments showed that upregulation of class I expression by these \*\*\*peptides\*\*\* was dependent on a high \*\*\*peptide\*\*\* concentration, since consistent upregulation could in no case be detected at concentrations below 10 mu-M. The class I binding \*\*\*peptides\*\*\* identified in the present study may be useful in the study of the CTL response to \*\*\*HPV\*\*\* in mouse model systems. The enzyme immunoassay used could facilitate the rapid search for class I binding \*\*\*peptides\*\*\* .

L188 ANSWER 17 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 5

AN 94:406226 BIOSIS

DN 97419226

TI Class I \*\*\*MHC\*\*\* - \*\*\*peptide\*\*\* interaction: Structural and functional aspects.

AU Ruppert J; Kubo R T; Sidney J; Grey H M; Sette A

CS Cytel, 3525 John Hopkins Court, San Diego, CA 92121, USA

SO Behring Institute Mitteilungen 0 (94). 1994. 48-60. ISSN: 0301-0457

LA English

AB The structural requirements for the interaction between antigens and class I molecules was investigated through the use of a quantitative assay to measure \*\*\*peptide\*\*\* binding to different \*\*\*MHC\*\*\* class I alleles. We determined the permissiveness of the main anchors reported by Rammensee and his group for \*\*\*peptide\*\*\* binding and defined an extended motif for \*\*\*peptides\*\*\* binding to the HLA-A2.1 allele, including the role of non-anchor positions. It was found that the main anchors were necessary, but not sufficient, for good binding. Certain non-anchor positions contributed significantly to overall binding and were referred to as secondary anchors. This finding allowed a better prediction of high affinity binding \*\*\*peptides\*\*\* selected from libraries of different viral and tumor proteins. Furthermore, our data allowed correlation of the structural requirements for binding of \*\*\*peptides\*\*\* with crystallographic data of the \*\*\*MHC\*\*\* molecule. In order to characterize allele-specific motifs for a larger number of alleles, the HLA-A alleles A1, A3, A11, and A24, which represent some of the most common alleles found in different ethnic populations, were chosen. Here, most motifs were found to be highly exclusive; however, HLA-A3 and A11 shared a common motif. The defined motifs were validated further by using naturally processed \*\*\*peptides\*\*\* . Those \*\*\*peptides\*\*\* were also synthesized and tested for binding to the appropriate HLA alleles, giving a binding affinity from 0.3 to 200 nM



for sequences of naturally processed \*\*\*peptides\*\*\*. Finally, a set of all possible 9-mer \*\*\*peptides\*\*\* from \*\*\*HPV\*\*\* 16 proteins were synthesized and tested for binding to the five class I alleles. For each allele, high affinity binders were identified, thus allowing for selection of possible \*\*\*peptide\*\*\* candidates for a CTL based vaccine.

L188 ANSWER 18 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:151455 NLDB  
TI \*\*\*Peptide\*\*\* Vaccination with a Cytotoxic T-Cell Epitope  
Derived from the \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\* \*\*\*Virus\*\*\*  
Type 16 Oncogene E7 Confers Protection Against \*\*\*HPV16\*\*\*  
-Induced Tumors  
SO Cancer Weekly, (26 Apr 1993) .  
ISSN: 0896-7384.  
PB CW Henderson, Publisher  
DT Newsletter  
LA English  
WC 359

L188 ANSWER 19 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.

AN 93:134063 NLDB  
TI Protection Against a \*\*\*Human\*\*\* \*\*\*Papilloma\*\*\*  
\*\*\*Virus\*\*\* Type 16 -Induced Tumor by \*\*\*Peptide\*\*\*  
Vaccination with a Cytotoxic T -Cell Epitope Derived from the Viral  
Oncogene E7  
SO Cancer Weekly, (19 Apr 1993) .  
ISSN: 0896-7384.  
PB CW Henderson, Publisher  
DT Newsletter  
LA English  
WC 296

L188 ANSWER 20 OF 31 CAPLUS COPYRIGHT 1995 ACS DUPLICATE 6

AN 1994:426884 CAPLUS  
DN 121:26884  
TI \*\*\*Peptides\*\*\* of \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
\*\*\*virus\*\*\* for use in \*\*\*human\*\*\* T cell response-inducing  
compositions  
IN Kast, Wybe Martin; Melief, Cornelis Joseph Maria; Sette, Alessandro  
D.; Sidney, John C.  
PA Rijksuniversiteit Leiden, Neth.  
SO PCT Int. Appl., 64 pp.  
CODEN: PIXXD2  
PI WO 9322338 A1 931111  
DS W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP,  
KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK,  
UA, US, VN  
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR,  
IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG  
AI WO 93-NL93 930504  
PRAI EP 92-201252 920505  
EP 92-203870 921210  
EP 93-200243 930201  
EP 93-200621 930305  
DT Patent  
LA English  
AB A \*\*\*peptide\*\*\* comprising an amino acid sequence derived from a  
\*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* )  
protein, wherein said amino acid sequence has the ability to bind to  
a human Major Histocompatibility Complex Class I mol., is claimed.  
The \*\*\*peptides\*\*\* may be used in prophylactic or therapeutic  
treatment of cervical carcinoma and other \*\*\*HPV\*\*\* -related  
diseases (no data). Nine-residue \*\*\*peptides\*\*\* derived from  
\*\*\*HPV16\*\*\* or \*\*\*HPV18\*\*\* E6 and E7 proteins which bound to  
HLA-A2.1, -A1, -A2.1, -A3.2, -A11.2, and -A24 mols. were identified.

L188 ANSWER 21 OF 31 USPATFULL

AN 93:89648 USPATFULL  
TI Covalent polar lipid- \*\*\*peptide\*\*\* conjugates for  
immunological targeting  
IN Yatvin, Milton B., Portland, OR, United States  
Stowell, Michael H. B., Pasadena, CA, United States  
Malkovsky, Miroslav, Madison, WI, United States  
PA State of Oregon, Portland, OR, United States (U.S. state  
government)  
PI US 5256641 931026  
AI US 92-911209 920709 (7)  
RLI Continuation-in-part of Ser. No. US 90-607882, filed on 1 Nov



1990, now patented, Pat. No. US 5149794

DT Utility

EXNAM Primary Examiner: Rollins, John W.

LREP Allegretti & Witcoff, Ltd.

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

GI 7 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 676

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods of facilitating the entry of \*\*\*peptides\*\*\* into cells and targeting such \*\*\*peptides\*\*\* to specific organelles within the cell. The invention provides methods for delivering and specific targeting of antigenically-active \*\*\*peptides\*\*\* to cells for the specific production of immunological reactivity against such \*\*\*peptides\*\*\*, as well as compositions and pharmaceutical compositions of matter comprising such \*\*\*peptides\*\*\*. This invention thereby provides improved methods for vaccine production and in vivo vaccination against pathogenic microorganisms. Methods for alleviating autoimmune disease and ameliorating tissue and organ transplant rejection using such conjugates are also provided.

L188 ANSWER 22 OF 31 USPATFULL

AN 93:84900 USPATFULL

TI Artificial viral envelopes

IN Schreier, Hans, Gainesville, FL, United States

Chander, Ramesh, Bombay, India

Stecenko, Arlene A., Gainesville, FL, United States

PA Univ. of Florida Research Foundation, Inc., Gainesville, FL, United States (U.S. corporation)

PI US 5252348 931012

AI US 92-923016 920730 (7)

RLI Continuation of Ser. No. US 90-600641, filed on 19 Oct 1990, now abandoned

DT Utility

EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Kishore, G. S.

LREP Saliwanchik & Saliwanchik

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

GI No Drawings

LN.CNT 731

AB The production of artificial viral envelopes by a novel double-detergent dialysis technique is disclosed. Specifically exemplified is the production of HIV-1 and RSV viral envelopes. The resulting artificial viral envelopes are essentially identical to the natural virus with regard to characteristics which are relevant to immunogenicity.

L188 ANSWER 23 OF 31 CANCERLIT

DUPLICATE 7

AN 93233248 CANCERLIT

TI Production and characterization of human proliferative T-cell clones specific for human papillomavirus type 1 E4 protein.

AU Steele J C; Stankovic T; Gallimore P H

CS Department of Cancer Studies, Medical School, University of Birmingham, United Kingdom.

SO J Virol, (1993). Vol. 67, No. 5, pp. 2799-806.

Journal code: KCV. ISSN: 0022-538X.

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDL; Cancer Journals; L; Priority Journals

LA English

OS MEDLINE 93233248

EM 9306

AB Human papillomavirus type 1 (HPV1) virions and E4 protein purified from cutaneous warts were tested in lymphocyte proliferation assays using normal individuals. Both antigens were found to be capable of eliciting good lymphoproliferative responses. Several T-cell clones specific for wart E4 protein were obtained from a donor who had consistently responded very well to E4 in these initial assays. They were maintained in culture by repeated stimulation with antigen and interleukin-2, using an autologous mitomycin-treated lymphoblastoid cell line as a source of antigen-presenting cells. Two of these clones (3F5 and 4A8), which behaved identically, have been studied in more detail. A series of overlapping synthetic \*\*\*peptides\*\*\* covering the entire E1 E4 protein sequence was used to identify a single T-cell epitope which maps to a strongly hydrophilic region spanning amino acid residues 38 to 50. We have also tested the ability of a panel of major histocompatibility complex class II-matched and -mismatched lymphoblastoid cell lines to present this \*\*\*peptide\*\*\* to the T-cell clones in proliferation assays. The



study reports that the epitope is restricted through HLA-DQ7 and that it can be recognized by T cells with different T-cell receptor gene rearrangements.

L188 ANSWER 24 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 8  
AN 93:480335 BIOSIS  
DN BA96:113935  
TI VACCINATION WITH CYTOTOXIC T LYMPHOCYTE EPITOPE-CONTAINING  
\*\*\*PEPTIDE\*\*\* PROTECTS AGAINST A TUMOR INDUCED BY HUMAN  
PAPILLOMAVIRUS TYPE 16-TRANSFORMED CELLS.  
AU FELTKAMP M C W; SMITS H L; VIERBOOM M P M; MINNAAR R P; DE JONGH B M;  
DRIJFHOUT J W; TER SCHEGGET J; MELIEF C J M; KAST W M  
CS DEP. IMMUNOHEMATOL. BLOOD BANK, UNIV. HOSP. LEIDEN, BLDG. 1 E3-Q,  
P.O. BOX 9600, NL 2300 RC LEIDEN, NETHERLANDS.  
SO EUR J IMMUNOL 23 (9). 1993. 2242-2249. CODEN: EJIMAF ISSN: 0014-2980  
LA English  
AB Cytotoxic T lymphocyte (CTL) \*\*\*peptide\*\*\* epitopes can be used  
for immunization of mice against lethal virus infection. To study  
whether this approach can be successful against virus-induced tumors  
we generated a B6 (H-2b) tumorigenic cell line transformed by  
\*\*\*human\*\*\* \*\*\*papillomavirus\*\*\* ( \*\*\*HPV\*\*\* ). This  
\*\*\*virus\*\*\* is detected in over 90% of all human cervical cancers.  
To identify vaccine candidates, we generated a set of 240 overlapping  
\*\*\*peptides\*\*\* derived from the \*\*\*HPV\*\*\* type 16 ( \*\*\*HPV16\*\*\* )  
oncogenes E6 and E7. These \*\*\*peptides\*\*\* were tested for their ability  
to bind H-2Kb and H-2Db \*\*\*MHC\*\*\* class I molecules. Binding  
\*\*\*peptides\*\*\* were compared with the presently known \*\*\*peptide\*\*\*  
-binding motifs for H-2Kb and H-2Db and the predictive value of these motifs  
is shortly discussed. The high-affinity H2Db-binding \*\*\*peptide\*\*\* and  
putative CTL epitope E7 49-57 (RAHYNIVTF) was used in vaccination studies  
against \*\*\*HPV\*\*\* 16-transformed tumor cells. Immunization with \*\*\*peptide\*\*\*  
E7 49-57 rendered mice insensitive to a subsequent challenge with  
\*\*\*HPV\*\*\* 16-transformed tumor cells in vivo, and induced a CTL response  
which lysed the tumor cells in vitro.

L188 ANSWER 25 OF 31 CAPLUS COPYRIGHT 1995 ACS  
AN 1993:227420 CAPLUS  
DN 118:227420  
TI Human YB-1 protein binding to enhancer of \*\*\*human\*\*\*  
\*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 18  
AU Spitkovsky, D. D.; Royer, H. D.; Mazurenko, N. N.; Mikhaleva, I. I.;  
Prudchenko, I. A.; Korbukh, I. A.; Sukhova, N. M.; Kissejov, F. L.  
CS Can. Res. Cent., Inst. Carcinogen., Moscow, 115478, Russia  
SO Mol. Biol. (Moscow) (1993), 27(1), 81-91  
CODEN: MOBIBO; ISSN: 0026-8984  
DT Journal  
LA Russian  
AB Enhancer sequences of \*\*\*human\*\*\* \*\*\*papilloma\*\*\*  
\*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) type 18 were used for screening of a  
HeLa cell cDNA library in .lambda. gt11 using the protein binding  
method. Clones with YB-1 gene homol. sequences were isolated. The  
gene codes for a protein which binds the regulatory region of gene Y  
for major histocompatibility complex class II (HLA 11). The YB-1  
transcripts were found in all samples of cervical carcinomas. To  
analyze the protein, rabbit antibodies were produced to a synthetic  
\*\*\*peptide\*\*\*, which corresponds to the most hydrophilic region of  
the protein. This antipeptide serum permitted identification of a  
nuclear 42K protein in HeLa cells as well as in normal fibroblasts.

L188 ANSWER 26 OF 31 COPYRIGHT 1995 INFO. ACCESS CO.  
AN 92:203772 NLDB  
TI MEDICAL GRANT MONITOR: A REGULAR UPDATE ON ALL MAJOR RESEARCH AWARD  
GRANTS--Allergy and Infectious Diseases  
SO Medical Research Funding News, (13 May 1992).  
ISSN: 1052-9152.  
PB Faulkner & Gray, Inc.  
DT Newsletter  
LA English  
WC 470

L188 ANSWER 27 OF 31 CAPLUS COPYRIGHT 1995 ACS  
AN 1992:590111 CAPLUS  
DN 117:190111  
TI \*\*\*Human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* \*\*\*peptides\*\*\*  
and organisms producing said \*\*\*peptides\*\*\* for use in vaccine  
compositions  
IN Thomas, Elaine Kinney; Chen, Lieping; Blake, James; Hellstrom, Karl  
Erik; Hellstrom, Ingegerd; Hu, Shiu Lok  
PA Bristol-Myers Squibb Co., USA



SO PCT Int. Appl., 82 pp.

CODEN: PIXXD2

PI WO 9205248 A1 920402

DS W: AU, CA, JP, KR, NO

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

AI WO 91-US7081 910926

PRAI US 90-588384 900926

DT Patent

LA English

AB Immunogenic \*\*\*peptides\*\*\* corresponding to \*\*\*peptides\*\*\* expressed in mammalian cells in response to \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* ( \*\*\*HPV\*\*\* ) infection are described. Recombinant organisms (such as vaccinia virus or tumor cells) producing such a \*\*\*peptide\*\*\*, or the \*\*\*peptide\*\*\*, can be used to treat \*\*\*HPV\*\*\* infections. Recombinant vaccinia virus expressing either the \*\*\*HPV\*\*\* E7 or E6 gene, and mammalian cell expression plasmids contg. these genes, were prepd. Mice were injected i.p. with \*\*\*HPV\*\*\* E7 epitope-producing fibroblasts, then challenged by s.c. administration of a tumorigenic dose of M2 melanoma cells transfected with \*\*\*HPV16\*\*\* E7 expression vector. A transient development of tumors followed by tumor regression was obsd.

L188 ANSWER 28 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 9

AN 92:501950 BIOSIS

DN BA94:120475

TI INDUCTION OF CYTOTOXIC T LYMPHOCYTES WITH \*\*\*PEPTIDES\*\*\* IN-VITRO IDENTIFICATION OF CANDIDATE T-CELL EPITOPES IN \*\*\*HUMAN\*\*\* \*\*\*PAPILLOMA\*\*\* \*\*\*VIRUS\*\*\*

AU STAUSS H J; DAVIES H; SADOVNIKOVA E; CHAIN B; HOROWITZ N; SINCLAIR C  
CS IMP. CANCER RES. FUND, HUM. TUM. IMMUNOL. GROUP, UNIVERSITY COLL., MIDDLESEX HOSP., LONDON W1P 8BT, UK.

SO PROC NATL ACAD SCI U S A 89 (17). 1992. 7871-7875. CODEN: PNASA6  
ISSN: 0027-8424

LA English

AB A set of overlapping \*\*\*peptides\*\*\* corresponding to the L1, E6, and E7 proteins of \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* 16 was tested for their ability to bind to \*\*\*major\*\*\* \*\*\*histocompatibility\*\*\* \*\*\*complex\*\*\* \*\*\*class\*\*\* \*\*\*molecules\*\*\* and to stimulate cytotoxic T-lymphocyte (CTL) responses in vitro. A class I binding assay using intact RMA-S cells showed that 20 of the 99 \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\* \*\*\*peptides\*\*\* bound to H-2Kb and/or Db molecules. Fifteen of the 20 class I-binding \*\*\*peptides\*\*\* stimulated primary CTL responses, whereas \*\*\*peptides\*\*\* that were negative in the binding assay failed to do so. \*\*\*Peptide\*\*\* -induced CTLs recognized the immunizing \*\*\*peptide\*\*\* very efficiently, requiring no more than 1-10 nM \*\*\*peptide\*\*\* for target cell lysis. However, two observations were made that have important implications for the design of \*\*\*peptide\*\*\* -based vaccines for inducing CTLs. (i) Not all major histocompatibility complex-binding \*\*\*peptides\*\*\* that contained known motifs characteristic of naturally processed \*\*\*peptides\*\*\* induced CTLs. (ii) The efficiency of CTL lysis was strongly decreased when the size of the target \*\*\*peptide\*\*\* differed by only one amino acid residue from that of the immunizing \*\*\*peptide\*\*\*. We conclude that \*\*\*peptides\*\*\* chosen for vaccination must correspond in length to naturally processed \*\*\*peptides\*\*\*.

L188 ANSWER 29 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 10

AN 92:282442 BIOSIS

DN BA94:7092

TI DEFINITION OF IMMUNOGENIC DETERMINANTS OF THE HUMAN PAPILLOMAVIRUS TYPE 16 NUCLEOPROTEIN E7.

AU ALTMANN A; JOCHMUS-KUDIELKA I; FRANK R; GAUSEPOHL H; MOEBIUS U;  
GISSMANN L; MEUER S C

CS DEP. APPLIED IMMUNOLOGY, INSTITUTE RADIOLOGY PATHOPHYSIOLOGY, IM NEUENHEIMER FELD 280, D-6900 HEIDELBERG, GER.

SO EUR J CANCER 28 (2-3). 1992. 326-333. CODEN: EJCAEL ISSN: 0959-8049

LA English

AB Specific T lymphocyte lines and T cell clones were established from peripheral blood mononuclear cells of asymptomatic seropositive individuals employing synthetic \*\*\*peptides\*\*\* which correspond to the sequence of the human papillomavirus ( \*\*\*HPV\*\*\* ) type 16 transforming protein E7. Specificity analysis of T cells as determined by means of [3H] thymidine incorporation after stimulation with individual \*\*\*peptides\*\*\* revealed three immunogenic determinants of E7 that are recognised in association with at least two different HLA haplotypes. One N-terminal region (aminoacids 5-18) was recognised by one T cell line. T cell clones and the corresponding T cell line established from another donor responded to



different N-terminal (17-38) and to a C-terminal region (69-86). The N-terminal sequence 5-18 and the C-terminal determinant contain a periodicity of hydrophilic and hydrophobic residues that have been found in many T cell epitopes. Phenotypic characterisation of T cell clones by indirect immunofluorescence revealed that the T cell clones expressed the CD4 surface glycoprotein suggesting that the specific E7 determinants were recognised in association with major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II molecules. With regard to functional properties, at least three T cell clones exhibited specific cytotoxic activity towards autologous B lymphocytes transformed by Epstein-Barr virus in the presence of the relevant \*\*\*HPV16\*\*\* E7 \*\*\*peptides\*\*\*. The implications of these results regarding the development of vaccination strategies and host-virus interaction are discussed.

L188 ANSWER 30 OF 31 CANCERLIT DUPLICATE 11  
 AN 92094170 CANCERLIT  
 TI T-CELL IMMUNOTHERAPY OF CANCER.  
 AU Melief C J; Kast W M  
 CS Division of Immunology, The Netherlands Cancer Institute, Amsterdam.  
 SO Res Immunol, (1991). Vol. 142, No. 5-6, pp. 425-9.  
 Journal code: R6E. ISSN: 0923-2494.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 FS MEDL; L; Priority Journals  
 LA English  
 OS MEDLINE 92094170  
 EM 9203  
 AB In animal systems, complete and permanent eradication of tumours can be achieved by adoptive transfer of \*\*\*MHC\*\*\* -restricted T cells, combined with IL2. In certain types of human cancer (melanoma and perhaps renal cell carcinoma), tumour-specific T cells are probably the therapeutically most active cells among LAK or TIL cells. To prove these points, it is necessary to conduct trials with cloned tumour-specific T cells. Other potentially immunogenic tumors are cervical carcinoma, associated with \*\*\*human\*\*\* \*\*\*papilloma\*\*\* \*\*\*virus\*\*\*, and Burkitt's lymphoma, associated with Epstein-Barr virus. Most other human tumours, caused by subtle mutations in proto-oncogenes, are likely to be poorly or non-immunogenic. It is worthwhile trying to overcome this by vaccination with IL2 or IFN gamma-producing tumour cells or by deliberate vaccination with desirable targets for tumour-specific CTL such as the products of point-mutated oncogenes, including ras (Jung and Schleusener, 1991) and p53 (Rodriguez et al., 1990; Halevy et al., 1990), provided the relevant \*\*\*peptides\*\*\* are processed and bound to \*\*\*MHC\*\*\* class I molecules. Other potential targets are breakpoint \*\*\*peptides\*\*\* of translocated oncogene products such as bcr/abl (Van Denderen et al., 1990). In viral systems, it has already been established that \*\*\*peptide\*\*\* vaccination for protective CTL induction is feasible (Aichele et al., 1989; Schulz et al., 1991; Kast et al., 1991). (46 Refs)

L188 ANSWER 31 OF 31 BIOSIS COPYRIGHT 1995 BIOSIS DUPLICATE 12  
 AN 91:49209 BIOSIS  
 DN BA91:27490  
 TI DEFINITION OF MURINE T HELPER CELL DETERMINANTS IN THE MAJOR CAPSID PROTEIN OF HUMAN PAPILLOMAVIRUS TYPE 16.  
 AU DAVIES D H; HILL C M; ROTHBARD J B; CHAIN B M  
 CS IMPERIAL CANCER RES. FUND TUMOUR IMMUNOL. UNIT, DEP. BIOL., MEDAWAR BUILD., UNIV. COLL. LONDON, GOWER ST., LONDON WC1E 6BT.  
 SO J GEN VIROL 71 (11). 1990. 2691-2698. CODEN: JGVIAJ ISSN: 0022-1317  
 LA English  
 AB Three murine major histocompatibility complex ( \*\*\*MHC\*\*\* ) class II-restricted T cell determinants were identified in the major capsid protein L1 of human papillomavirus ( \*\*\*HPV\*\*\* ) type 16. \*\*\*Peptides\*\*\* derived from \*\*\*HPV\*\*\* -16 L1, which contain putative T cell epitopes located by a predictive algorithm, were synthesized and tested for lymphoproliferative activity by direct immunization, followed by in vitro assay of responses to \*\*\*peptides\*\*\* or recombinant \*\*\*HPV\*\*\* -16 L1. The \*\*\*MHC\*\*\* restriction of the stimulatory \*\*\*peptides\*\*\* was determined using blocking monoclonal antibodies against class II molecules. The responses, which were specific for the priming \*\*\*peptides\*\*\* alone, cross-reacted with recombinant L1 but not with analogous \*\*\*peptides\*\*\* derived from other \*\*\*HPV\*\*\* types.